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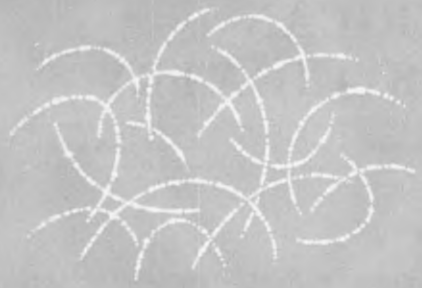
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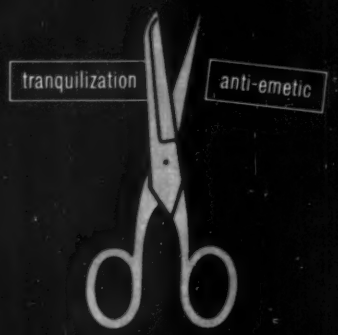
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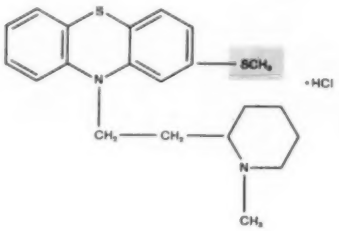
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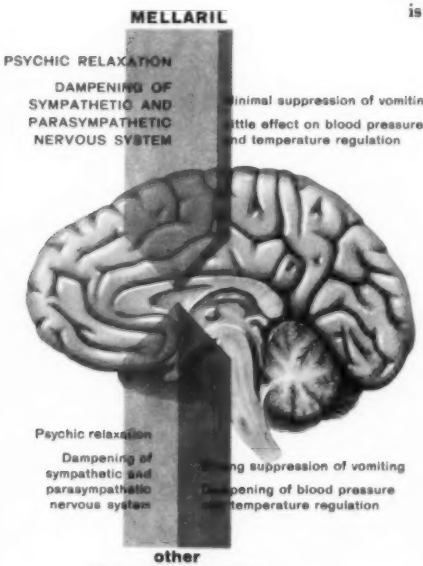


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SCHIZOPHRENIA				
Acute	89	61	28	11
Chronic paranoid	84.2	31.6	52.6	15.8
Chronic, other	73.9	21.7	52.2	26.1
Residual	57.1	9.5	47.6	42.9
CHRONIC BRAIN SYNDROME	66.6	33.3	33.3	33.3
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1. Ostfeld, A. M.: Scientific Exhibit, American Academy of General Practice, San Francisco, April 6-9, 1959. 2. Kinross-Wright, V. J.: Lecture, Clinical Meeting, American Medical Association, Minneapolis, Dec. 4, 1958. 3. Kinross-Wright, V. J.: Scientific Exhibit, Clinical Meeting, American Medical Association, Minneapolis, Dec. 2-5, 1958. 4. Cohen, S.: TP-21, a new phenothiazine, Am. J. Psychiat. *115*:358, Oct. 1958. 5. Glueck, B.: Scientific Exhibit, American Psychiatric Association, Philadelphia, April 27-May 1, 1959. 6. Hollister, L. E., and Macdonald, B. F.: Presented at California Medical Association; Section on Psychiatry, San Francisco, Feb. 25, 1959. 7. Remy, M.: Schweiz. med. Wchnschr. *88*:1221, Nov. 29, 1958. 8. Freed, S. C., in discussion on Thioridazine (Mellaril) in Psychiatric Patients, Hollister, L. E., and Macdonald, B. F., presented at California Medical Association; Section on Psychiatry, San Francisco, Feb. 25, 1959.

- controls neurotic and psychotic patients with anxiety, apprehension, nervous tension
- virtual absence of jaundice, parkinsonism, photosensitivity, dermatitis
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1. Ehrmantraut, W., et al.: Scientific Exhibit Presented at the District of Columbia Medical Society Meeting, Nov. 24, 1958, Washington, D.C.

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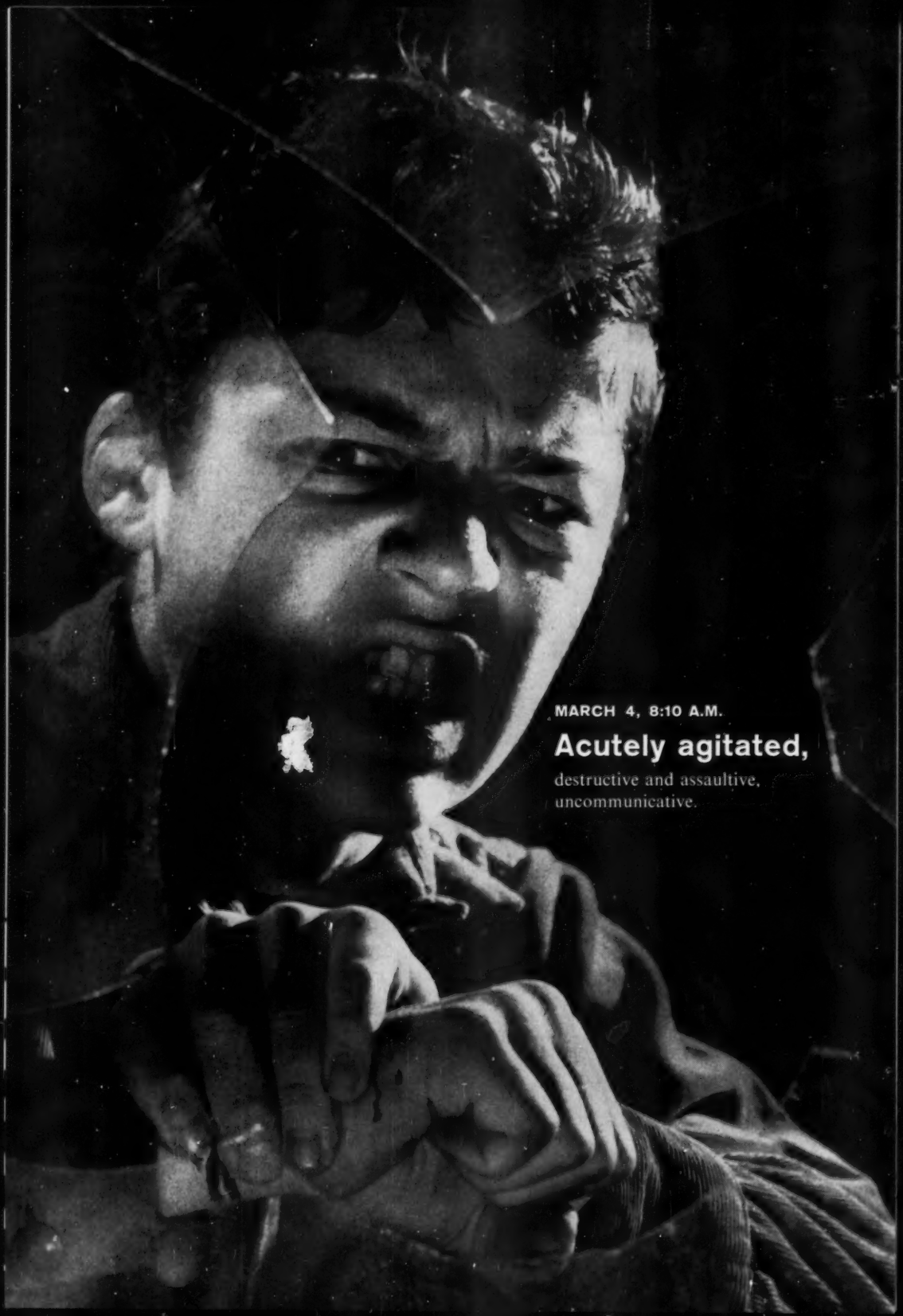
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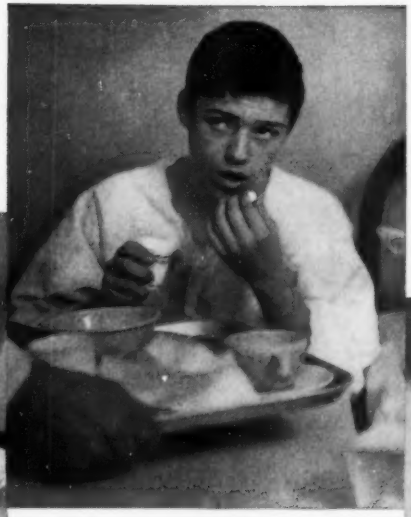
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Acutely agitated,
destructive and assaultive,
uncommunicative.



MARCH 4, 10:00 A.M.
SPARINE, I.V., has been given.
Patient in light sleep.
Can be awakened readily,
and responds to questioning.



MARCH 5, 2:00 P.M.
Receiving oral SPARINE.
Quiet but alert. Contrite
about smashed window.



MARCH 8, 9:00 A.M.
Still on oral
SPARINE, maintenance
dosage. Ready
for psychotherapy.

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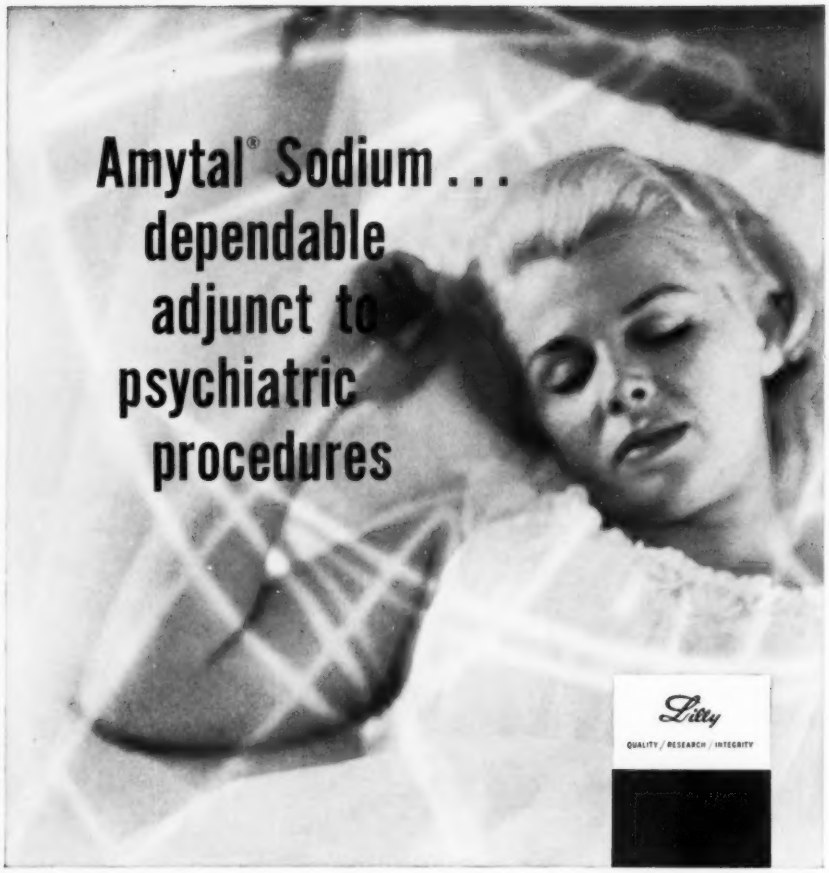
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RELATION BETWEEN HISTORY, PERSONALITY AND FAMILY PATTERN AND BEHAVIORAL RESPONSE AFTER FRONTAL LOBE SURGERY[1]

MILTON GREENBLATT, M.D.[2]

The lobotomy studies of the psychosurgical period afforded an excellent opportunity to investigate the relationship between behavior after brain damage and a large number of variables related to history, personality, and background.

For the purposes of our discussion, it would be most fortunate if the frontal section produced by the operation were uniform from patient to patient. Unfortunately, this is not so. Even where the surgical intent is the same, and the procedure held, as far as possible, constant, the lesion probably varies considerably. Skulls vary, brains vary anatomically and functional organization—whatever there is of it in the frontal lobes—also varies. A conservative surgeon has stated that with the best planning the plane of the section could easily vary by as much as one centimeter. Clearly this could make a tremendous difference in the pattern of fibers cut and in the ultimate reorganization of personality in response to brain lesion.

In my first discussion I will draw upon a series of cases of chronic psychosis from lobotomy studies carried out between 1943 and 1949(1). During this period the operative lesion was a full bilateral cut performed *via* a superior opening just anterior to the saggital suture with all technical procedures under direct visualization (Poppen's technique). A careful analysis of traits or "factors" was done before and after operation. Thirty factors were studied, selected on the basis that each was relatively objective, readily observable, and could be easily rated or quantified. In speaking of the changes, we think of them as changes "following operation" rather than caused by operation. This seems like reasonable, scientific caution, since changes under these circumstances are complexly determined.

One of the most important discoveries of this study was that with almost all factors there appeared a shift in two directions: a group of patients who were "abnormal" in respect to a trait becoming "normal" after operation; and, conversely, a group who were "normal" before operation becoming "abnormal" after operation. Our data are based on 181 patients followed up 1 to 4 years after surgery. In some instances, the abnormal characteristics existing preoperatively disappeared altogether postoperatively with no symptom of this type appearing in any cases for the first time following operation. In other instances, the abnormal symptom receded markedly or disappeared postoperatively in a large percent of the cases but appeared for the first time in a small percent of cases; and in a final group, the shift in the normal direction was more than overbalanced by a shift in the abnormal direction.

Figure 1 illustrates those areas where, in our experience, the most reliable prediction of change in a favorable sense may be made. Virtually no patient developed postoperatively the symptom or trait designated, and a very large proportion of those who had these traits preoperatively were relieved by operation. If this were the sum total of changes produced, certainly lobotomy would be more popular today than it is.

Let us now turn our attention to a group of manifestations that are to a large degree improved by operation but where there is a definite risk of producing an undesired change postoperatively as well.

Figure 2 shows 5 factors in which there is not only expectation of good results, but also a chance that undesirable changes will occur, too. In the case of "Alcoholic Excess," of 6 patients who could be put

[1] Read at the 114th annual meeting of The American Psychiatric Association, San Francisco, Calif., May 12-16, 1958.

[2] Assistant Superintendent and Director of Research & Laboratories, Massachusetts Mental Health Center (Boston Psychopathic Hospital); and Associate Clinical Professor of Psychiatry, Harvard Medical School, Boston, Mass.

FIGURE 1

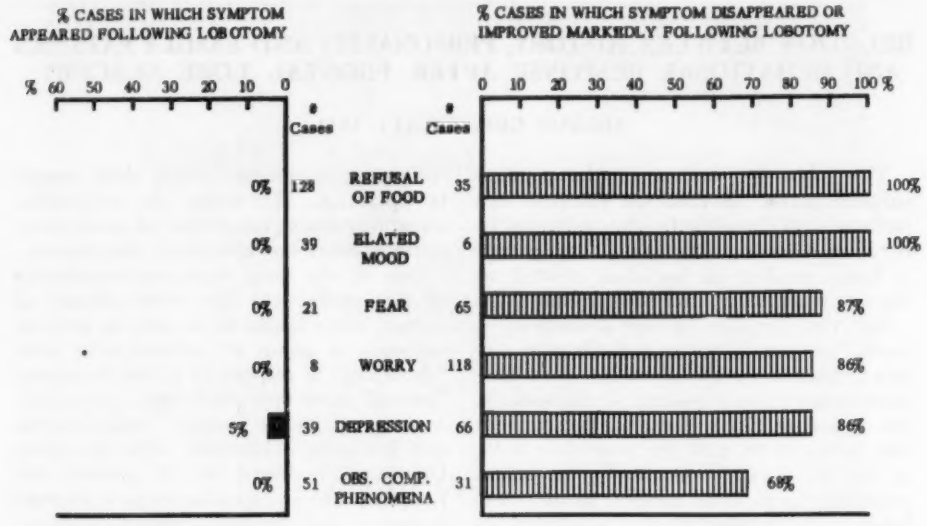
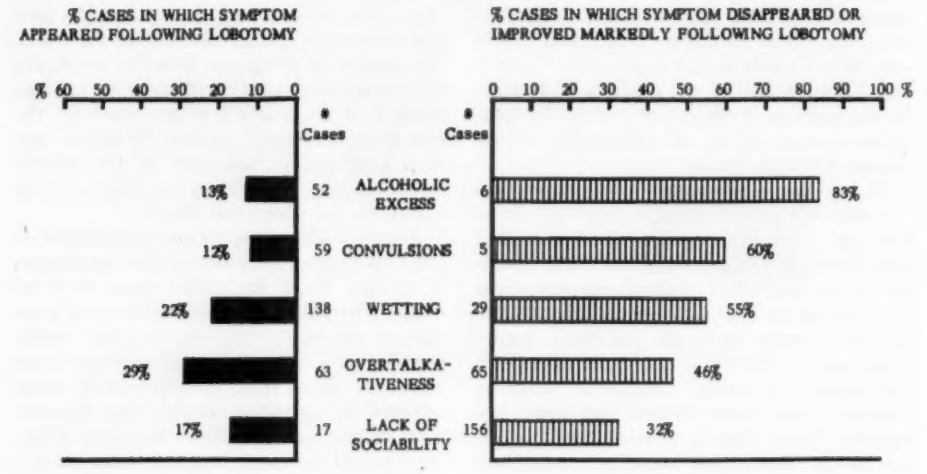


FIGURE 2



in this category preoperatively, 5 were relieved entirely of their alcoholism postoperatively. However, of 52 who were clearly non-indulgent, 7 (13%) increased their consumption significantly postoperatively. In a separate publication(2) we studied in detail the question of alcoholism in a larger series of cases with the following conclusions: 93% of lobotomized patients who returned to the community did not change their drinking habits. Those who did usually changed markedly, going from one extreme to the other. Five patients (3%) out of 167 non-alcoholics became alcoholic for the first time after lobotomy. Three (25%) out of 12 known alcoholics stopped drinking entirely. Four (33 1/3%) of the 12 drank more after lobotomy than previously; and 5 (41%) were unchanged in their drinking habits.

The social problem of the small group who drank excessively, however, was often severe since they were less tolerant of alcohol, more hostile, insensitive and anti-social.

It is interesting to know that although in this group the risk of convulsions after operation was in the neighborhood of 12%, nevertheless 5 of 6 well-established epileptics were markedly improved in terms of the frequency and severity of seizures. In the former, the convulsions may be understood as at least partly "caused" by brain damage; in the latter, our hypothesis is that convulsions were related to tension and emotional difficulties which were allayed by operation.

With wetting, which has been defined as incontinence (frequent or infrequent, one month or more after operation) some 22% of patients formerly continent became wetters, yet 55% of those who were wetters as part of their psychotic state were relieved of this symptom.

The next 2 items, overtalkativeness, and lack of sociability, reflect lack of social refinement and restraint commonly found in patients after full bilateral operations.

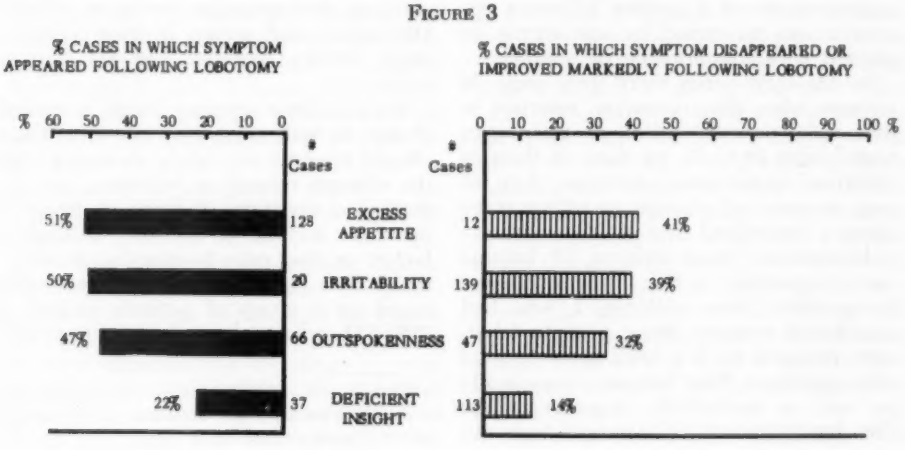
Figure 3 shows 4 areas in which the degree of improvement is overshadowed by the production of undesirable effects. We find that excess appetite, irritability, outspokenness, and deficient insight are more often produced than reduced by operation.

Thus, psychosurgical treatment must be understood in terms of its double potential —to "normalize behavior" and to "abnormalize" behavior. Changes clearly can go in different directions and "undesirable" manifestations in a given dimension may be more pronounced than "desirable" manifestations. This terminology inevitably involves us in the problem of *evaluation* of change, a complex matter that cannot be considered fully here. The issue, however, is so important as to warrant discussion in at least one of its dimensions of consideration.

We have learned that the degree of satisfaction felt as the result of given personality changes following psychosurgery is in large measure a function of family dynamics. For example, some 25 cases were studied where after operation a husband or wife returned to live with the spouse. Many of the changes in family relationship in this context could be seen as subsequent to changes along theoretical "aggression-submission" axis. It was possible to demonstrate that in some instances the husband-wife relationship was rendered more comfortable and, in other instances, less comfortable by a shift in the spouse, either towards the aggressive or towards the submissive end of the continuum.

Thus, Mrs. K, a 70-year-old, married, childless woman, had considerable drive, energy and responsibility, while her husband who was unambitious did odd, unskilled jobs

FIGURE 3



around the house and drank a good deal. Mrs. K met interesting, influential people on her job and received much attention because of her pleasing personality. At home she was the "boss" of the family. However, when her job was terminated during an economic depression, she promptly fell into an agitated state, full of anguish, hand-wringing and pacing. This lasted undiminished for 8 years.

Following operation, all symptoms disappeared but unfortunately the patient took little interest in her appearance, her job or her housework. She seemed content and relaxed and turned over all responsibilities to her husband who in turn was delighted by the change, joyfully accepted the new duties, did not complain of her laziness, and even stopped drinking. The decrease in energy and tension of his wife seemed to give him the feeling of adequacy and masculine dominance he needed.

By contrast, consider the H family in which the wife was almost the twin of Mrs. K—elderly, childless, domineering, energetic and successful before the onset of her illness which was characterized by crying, somatic complaints and agitation. After operation she was lacking in energy or initiative. Her husband complained, "She is hopelessly lazy; I might as well be a bachelor." He grudgingly did the housework, cooking, *etc.*—all the things that Mr. K had enjoyed. He became disgruntled, thin, unhappy ; but his wife was cheerful and no longer wept. She seemed content although she expressed some dissatisfaction concerning her lack of energy.

Similar examples could be quoted illustrating how an *increase* in energy and aggressiveness of a partner following operation was welcomed by one spouse or greeted with consternation by another.

In our early series there were some 36 patients who, after operation, returned to live with parents. Although their ages varied from 16 to 45, we think of them as "children" in the family structure. Here we may conceive of changes as taking place along a theoretical axis of "dependence—independence." Most children, 33, became more dependent ; a few, 3, became more independent. Some children, 7, who had established separate living prior to lobotomy returned to live with their families after operation. They became economically as well as emotionally dependent upon their families which led to more disturbance than in those instances where patients had formerly lived with parents and after operation returned to the same setting.

Among the instances of increased independence may be mentioned :

One attractive manic-depressive female became engaged, married and moved to another state where she adjusted well.

One passive-submissive son for the first time after operation was able to voice his antagonism to his father to the surprise of his parents, and one day, in typical Hollywood fashion, he made a dramatic exit from the family home in the middle of a blizzard. The patient has been self-supporting and said, "It made a new man out of me." He has never been reconciled with his father.

The third patient lived with the mother who died while she was hospitalized. After trying unsuccessfully to live with her brother, she then made it alone in a rooming house, supporting herself on her own job, even receiving a raise.

Parents of younger children may be considered in the light of how well they reared their offspring after operation. Our best data concern a group of 14 mothers studied by Greta Sharaf(3). Of these, 5 fulfilled the role adequately, 3 partially, and 6 failed completely. These 5 are of special interest apropos the question of the effect of radical brain lesions on maternal behavior. It may be surprising to some that two parents formerly preoccupied with obsessive details, cleanliness, and self-imposed standards so as to be unable to care for children, after operation were more relaxed, affectionate and secure in their relationships. Others, however, did not fare as well.

We see above opposing trends in clinical change as well as varying effects of these clinical changes on family dynamics. Are the changes related to fortuitous and uncontrolled variations in plane or extent of operative section, or are they related to factors existing prior to operative intervention ? Data from social interaction studies based on a group of patients studied in 1950-53 [3] indicate dependence of postoper-

[3] These cases received different kinds of operation —bimedial, bilateral, and unilateral frontal sections by the Poppen method.

tive changes in behavior on preoperative characteristics of *social interaction*.

Investigations carried out by J. S. Bockoven(4) on the interaction of patients in an occupational therapy situation both pre- and postoperatively provide us with a clue to social changes for this particular population. First, the overall results.

> The results indicate that the statistically average patient increased interaction with his environment after frontal lobe surgery. Specifically, he talked and read more, increased in responsiveness and steadfastness, and carried out more organized actions. He also socialized more with other patients, but showed no change in socialization with hospital personnel; he tended, however, to be more friendly. On the whole the study indicated the average patient became a more active and expressive group member following frontal lobe surgery(5).

Now, what is the relationship between preoperative social behavior and postoperative change? For want of time, I present very briefly the complex findings of Bockoven:

(a) Patients who before operation manifested erratic, constantly shifting, overproductive motor activity, after operation generally moved towards lower energy output and more socially *relevant* activity. However, when the level of energy and activity was extremely low beforehand, there was a release of socially relevant action after operation.

(b) Patients who before operation were characterized as responsive, friendly, organized in their actions, and inclined to interact with other patients, generally showed great gains in these same characteristics after operation. However, those who were over-responsive, and over-friendly (whose over-sociability was in itself a symptom of a personality disorder) decreased in these manifestations after operation.

(c) The amount of reading after operation bore a reverse relationship to the preoperative tendency to read. Our interpretation is that excessive attention to reading in some instances is a technique of withdrawal from social activity. On the other hand, an increase in reading was noted for those who read very little—in this case, perhaps the first step in moving toward contact with their environment.

(d) Verbal activity on the whole tended to increase after operation and this in direct relationship to the level before operation.

These complex trends may be crudely summarized by saying that there is, in general, a normalizing tendency. Patients with excessive activity of a non-social type moved towards more socially acceptable behavior as did patients with a marked deficiency in social activity.

Some of the studies from the Massachusetts Mental Health Center have been relevant to the problem of prediction of outcome following surgery. Research-wise this has taken the form of exploring the relationship between specific variables identified before operation and mental status—good, fair, or poor—one year or more after operation. The patient with "good mental status" was one who showed no abnormality in the interview situation and was adjusting satisfactorily in his environment. "Fair mental status" indicated that relatively minor or mild abnormalities in thinking or behavior were present (for example, mild obsessive-compulsive trends or inconstant ideas of reference). "Poor mental status" indicated that the patient had gross defects in mental functioning, such as frank delusions, hallucinations, or deficient memory.

In 1950(1) and again in 1953(6), we published data summarizing our findings on prediction. In the 1950 publication, some 81 factors were correlated with improvement 1 to 4 years after operation, and in 1953 an even larger number of variables were analyzed. I have attempted to boil down the results of both studies and extract only those variables or factors which are of greatest value in prediction. Since the statistical approach in the two studies differed slightly, I am using a fair measure of personal judgment in selecting the variables. Our 1950 publication carries an interesting profile of the characteristics of a theoretical patient most likely to succeed and one least likely to succeed following operation. However, what I present here represents a more refined precipitate of our findings.

The table shows that with respect to

TABLE 1

PREDICTIVE FACTORS FOR

	IMPROVED CASES	UNIMPROVED CASES
ONSET OF ILLNESS	RAPID (ONE MONTH OR LESS)	INSIDIOUS
MANIFESTATIONS DURING ILLNESS	1. AUDITORY HALLUCINATIONS ABSENT 2. INSIGHT PRESENT 3. HIGH "TENSION"	1. AUDITORY HALLUCINATIONS PRESENT 2. INSIGHT ABSENT 3. LOW "TENSION"
DIAGNOSTIC CATEGORY	PSYCHONEUROSIS--- HYPOCHONDRIASIS OR OBSESSIVE-COMPULSIVE	DEMENTIA PRAECOX--- CATATONIC OR PARANOID CHRONIC MANIC
SOCIAL BEHAVIOR	1. MORE VERBAL 2. MORE FRIENDLY	1. LESS VERBAL 2. LESS FRIENDLY

manifestations during illness, *rapid onset* was highly predictive of good outcome as was *absence* of auditory hallucinations, the *presence* of insight and *high tension.*

As for diagnostic category, hypochondriasis and obsessive-compulsive psychoneurosis cases were most likely to improve ; however, dementia praecox, catatonic type or paranoid type (essentially chronic), or chronic manic cases, which are probably really variants of schizophrenia, did poorly. In social behavior, those patients who were *more verbal* and *more friendly* tended to improve, while those who were less verbal and less friendly failed to improve generally.

These factors, as we have indicated, were outstandingly helpful in prediction of outcome. Many other factors were helpful in prediction but at a lower level of reliability. For example, if one were married, had children, had obtained a higher education, and if it were possible to identify major precipitating factors in the illness, one was likely to be more helped by operation than if the reverse were true. Patients free of brain damage tended to have better prognosis than those who had brain damage. However, the mere presence of brain damage, if the clinical syndrome featured tension, *etc.*, did not preclude a good result. A good family, work and community adjustment before operation likewise was of predictive value. The profile thus described in 1950 correlates quite strikingly with the profile recently developed in independent research by Jaco (7, 8) in Texas, and is highly consistent with the findings over many years of our great American pioneer in psychosurgery, Dr. Walter Freeman(9, 10, 11).

It is also interesting to know that relatively good psychological organization, relatively high initiative, good abstraction in psychological tests and an ability to express dissatisfactions in free association were to some extent correlated with good outcome.

In the social sphere, although verbalness and friendliness were the most favorable items, many others at a lower level of predictive value could be mentioned ; for instance, ability to express positive and negative affect, or positive orientation to the group versus isolation—in other words, factors that taken together suggest preservation of social extrovertism.

In this communication I do not have time to mention our physiological analyses and the predictive power of straight physio-

logical testing. We were struck by the fact that physiological variables were, on the whole, quite predictive of outcome and feel that this area promises concrete help in our clinical work.

Summary

Studies of many patients before and after lobotomy indicate complex relationships between history, personality and behavioral response after frontal lobe surgery. It has been shown, for example, that postoperative changes may move in either direction along a given parameter—sometimes favorable and sometimes unfavorable. For example, worry and fear were greatly allayed after operation, yet not produced at all by operation. On the other hand, outspokenness existing before operation was removed as a symptom in one-third of the cases after operation, yet in a half of the cases in which it was of no significance preoperatively, outspokenness was *produced* as a postoperative, undesired characteristic.

It is possible to illustrate poignantly how a given change, such as an increase in aggressiveness or dominance, in some instances pleased the family, and in others caused constraints. Conversely, a decrease in aggressiveness or dominance could either please or displease the important persons in the patient's family circle. Social interaction studies showed that there was considerable dependence of postoperative change on preoperative level or type of socialization. In general, the tendency was towards a normalization of behavior: patients who showed excessive activity became more moderate, and patients with deficient activity tended to have a release of this activity after operation.

Concerning the problem of prediction of mental status after operation, it was noted that the primary predictors of good outcome were *rapid onset, high tension, insight present, hallucinations absent, verbalness and friendliness*, and, finally, a diagnosis of psychoneurosis rather than schizophrenia.

The experience suggests that the reactions to severe brain cutting are not to be predicted alone on the basis of the type and amount of brain cut or destroyed, but in relation to many factors from the background and personality of the patient.

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APPENDIX

Definition of Terms

Alcoholic Excess

a. Not present: a teetotaler, moderate drinker, or alcohol "not a problem."
b. Present: repeated drunkenness causing interference with satisfactory adjustment.

Convulsions

a. Absent: no epileptiform seizures.
b. Present: one or more epileptiform seizures.

Fearfulness
a. Normal: anxiety or tension consistent with reality threats.
b. Abnormal: constant anxiety or tension out of proportion to reality threats.

Food Intake
a. Normal: three meals a day without urging or numerous requests for supplementary food.
b. Inadequate: requires urging, prodding, or tube feeding.
c. Excessive: large meals plus insistent requirement of supplementary feedings.

Insight
a. Normal: patients recognized something wrong with them, that problems were psychological or emotional rather than physical; the patient formulated a chief complaint.
b. Abnormal: patient did not recognize anything was wrong with him. He did not make a chief complaint.

Irritability
a. Normal: irritation appropriate to the situation.
b. Abnormal: frequent annoyance disproportionate to the stimulus or situation.

Mood
a. Normal: absence of abnormal moods defined below.
b. Elated: obvious marked euphoria, with accompanying gush of speech, with or without overactivity.
c. Depressed: subjective admission of unhappy affect; patient looked depressed.

Obsessive-Compulsive Phenomena
a. Present: phenomena such as hand washing, overmeticulosity, or obtrusive possessing thoughts, such as fear of syphilis or germs.
b. Absent: judged to be within normal limits.

Sociability
a. Normal: friendly, outgoing.
b. Lacking: seclusive, withdrawn, avoided normal contacts.

Talkativeness
a. Normal: near-average number of interchanges; neither reticence nor pressure of speech.
b. Under: mute or monosyllabic.
c. Over: constant chatter; unusually rapid flow of speech.

Wetting
a. Absent: patient not a bed-wetter, not incontinent one month or more after lobotomy.
b. Present: patient either frequent or infrequent bed-wetter, or incontinent one month or more after lobotomy.

Worry
a. Normal: concern over reality issues proportionate to their importance.
b. Abnormal: constant distressed, disproportionate concern.

DISCUSSION

E. Gartly Jaco, Ph.D. (Galveston, Tex.)—The social dimension in psychiatric treatment has too often been ignored and Dr. Greenblatt is taking a forward step in presenting evidence relating such social factors as family background and social interaction to outcome of frontal lobe surgery.

There is, however, a point to keep in mind about prognosis, particularly with regard to psychosurgery. The group of patients exhibiting a favorable response to psychosurgery as reported in this paper are likely to respond well also to other forms of treatment. Consequently, until controlled comparisons are made between the various forms of lobotomy and other types of treatment, evaluation of psychosurgery as a mode of treatment more advantageous than less severe forms would be hazardous. This was one of the major reasons why a long-term investigation of patients administered transorbital lobotomy, and other types of somatic and drug therapy was initiated in several of the state mental hospitals in Texas several years ago. In comparing matched groups of cases in 3 of these institutions, the outcome both in and out of the hospital of 3 major forms of somatic treatment were studied. It would not be premature at this time to state that within 3 years of follow-up transorbital lobotomy has been the most successful in keeping patients out of the hospital, with chlorpromazine next best, while electroshock and deep insulin, along with custodial care were the least effective.

However, there is another social dimension that I would suspect is operating and affecting the differential outcome of various forms of psychiatric treatment, particularly as it is investigated in psychiatric research. This is what I would call the "faith-coefficient" operating in psychiatric treatment. There is an inherent risk in psychosurgery in adopting the typically "detached" attitude of the surgeon's relationship to his patients, and forgetting the therapeutic

aspects of the psychiatrist-patient relationship. Differences and results in treatment research may be due to differences in the degree of faith, that is, the amount of enthusiasm for and belief in the efficacy of the mode of treatment exhibited to the patient by either the therapist or researcher, which the therapist possesses in their modes of treatment, which in turn influences the patient and his belief in the therapeutic abilities of his therapist. One might hypothesize that the more enthusiastic the therapist is about his own modes of treatment, the more successful, in turn, such treatment will be for his patients. I think this is one of the reasons why certain therapists and researchers obtain different results in various forms of treatment than other therapists and researchers having greater skepticism for such treatment.

Consequently, the attitude toward psychosurgery and actually doing something for the patient—the process of preparation for lobotomy of both the patient and his family and other interested and significant members of his social milieu—may explain, in part, why some cases exhibited "abnormal" behavior which was "normal" before the operation, or *vice versa*. We would thus inquire of Dr. Greenblatt as to whether or not the group of patients analyzed in this study voluntarily went into psychosurgery, or were coerced, or simply disinterested. It is likely that the voluntary group would have a better outcome or reaction to psychosurgery than the involuntary groups of patients, particularly if any negativistic attitudes were displayed toward the involuntary group by the treatment staff. To some extent, such may be at least a partial explanation for the worsening of such characteristics as excessive appetite, irritability, outspokenness, and deficient insight in one of the series presented.

In summary, Dr. Greenblatt and his associates are to be congratulated in presenting a new series of dimensions of a social nature that affect the outcome of psychosurgery, an area in considerable need of further research in not only frontal lobe surgery, but every other form of psychiatric treatment. Until such factors as the "faith-coefficient" and other social and cultural dimensions are controlled or at least delineated, differential outcome in psychiatric research of various modes of therapy will continue to persist in the psychiatric literature. These social intervening variables, therefore, are worthy of inquiry in their own right, as well as in conjunction with improving our knowledge of and skills in psychiatric treatment.

REPLY

Milton Greenblatt, M.D., (Boston, Mass.).—One of our greatest areas of ignorance has to do with the relative efficacy of various forms of treatment in similar case groups. Until definitive studies are done of the type mentioned by Jaco, we will continue to depend on inference and prejudice. Successes are being claimed in chronic cases for all types of therapy used. What we need desperately to know is the spectrum of improvement to be expected with a given therapeutic modality in relation to others; the social and psychological conditions under which the improvement is obtained; the degree to which improvement is maintained versus relapse or regression; and finally, the relative costs of the various treatment methods.

I am personally not surprised to hear that transorbital lobotomy ran ahead of chlorpromazine, electric shock treatment, insulin treatment, and custodial care. Our recent experience is relevant. We studied comparable groups of chronic schizophrenics—one group remaining in a state hospital environment and given tranquilizers, the other group transferred to an active social milieu and given the same drugs. The results indicate that improvement rates are about the same after six months in the two environments, but that patients in the active milieu are more likely to leave the hospital because of social work attention and the use of transitional facilities. The significant feature for our discussion here, however, is that tranquilizer therapy does not appear to give as good results as psychosurgery in our estimation. Unfortunately, this is based on *impression* as we have not run *concurrent* matched or randomized groups with the different modalities. But we are intrigued with Jaco's statements which support our expectations.

I cannot give a satisfactory answer to the question as to whether those who volunteered did better than those who resisted surgery, simply because we kept no systematic data on this point at the time. His criticism is well taken, however, and were we to repeat the studies, we should certainly take this into account. Many of our patients were operated without any particular bones being made about

the operation. Some, to be sure, resisted. Many were so regressed and uncommunicative that their feeling about operation was unknown. Improvements occurred in all classes of individuals, however, but with a major positive correlation in our study between a clinical picture featuring tension, agitation, or what we might call "heightened cerebral excitation" and postoperative improvement.

In recent years we have done a good deal of work on the social components in therapeutic management of the mentally ill and have learned to respect the importance of the social milieu or setting as a variable affecting therapeutic outcome. The informal, subtle, or implicit aspects of the environment are especially tricky to identify, but we believe they may have a profound effect on patient care and treatment.

We wish to thank Dr. Jaco for emphasizing these most important aspects of the total problem.

PAVLOVIAN CONTEMPORARY PSYCHIATRY IN THE USSR[1]

KONSTANTIN M. BYKOV

LATE MEMBER OF THE ACADEMY OF SCIENCES OF THE USSR

Biology lies at the basis of modern medicine. The laws of biology are the foundation stones of the theory and practice of medicine. Man in all his complexity, as the object of medicine, should be dealt with on a humanitarian basis—psychological, sociological, *etc.*

All attempts to create a theoretical basis for medical science *only* on biology or *only* on psychology lead to a vulgar mechanistic system, and finally to an empty idealism.

Psychiatry, like every science, reflects in its development all those general premises of a scientific world outlook that prevail at a given period of history.

Before the beginning of this century, both in the field of neurology and of psychiatry, the views of the physiologists predominated, founded mostly on analytical physiology. These had been elaborated by means of vivisection, that is, by experiments with organs and tissues studied separately without any connection whatever with the higher psychic manifestations, mostly through subjective psychology, *viz.* unscientifically.

In a brief paper it is impossible to dwell at length upon the many attempts in building up new notions of the functions of the higher nervous apparatus governing the relationship between the organism and its environment. At the beginning of our century, efforts were made to found new concepts based on the correlation between psychopathology and pathological brain anatomy (Kleist, Pötzl, Meynert, Wernicke). Among Russian psychiatrists, some propagated this so-called "brain pathology," ignoring the importance of Pavlov's researches on the functions of the higher parts of the brain.

Some Russian psychiatrists, as well as those of other countries, made theoretical use of recent physiological concepts, such as those concerning integration and disintegration; the founder of these concepts was the prominent English physiologist Charles Sherrington. But that theory cannot adequately be adapted to psychiatry, for Sherrington and his followers in Western Europe, as well as in America, did not take into consideration the specific characteristics of the functions of the higher divisions of the central nervous system, nor the evolution of functions in their ascending order, *i.e.* adaptability and mutability, heredity and the individual experiences acquired during the individual's life.

The teachings of the behaviorists could not adequately represent the mechanism of normal brain activity, nor its pathological conditions. Behaviorist psychology defines only the beginning and concluding links in an act. The main intermediary, the central mechanism, remains thus unavailable to scientific investigation. In Lashley's ideas one can detect, however, a vague notion about the equipotentiality of the separate parts of the brain, founded upon a rather rough method of extirpation and upon a subjective point of view.

The brilliant work of Walter Cannon on the emotions, dealing with the role of adrenalin, and the research studies on the hormones, were isolated from general questions of physiology and pathophysiology. Endocrinology having been separated from the study of the organism as a whole, led some endocrinologists and physicians to erroneous inferences about the autonomic roles of separate hormones in the activity of an organism (Selye *et al.*). Hormones when exerting their influence, in our opinion, are still dependent upon the brain apparatus common to man and the other higher animals.

In many other countries the understanding of Pavlov's psychiatry and his research on the conditional reflexes is far from correct. Nor has adequate recognition been given to Pavlov's statement that with that development of the cerebral cortex found only in man, there appeared a higher function, the second signaling system, *i.e.* the

[1] Read at the 114th annual meeting of the American Psychiatric Association, San Francisco, Calif., May 12-16, 1958. Translated by W. Horsley Gantt, M.D., VA Hospital, Perry Point, Md.

speech function—at the basis of thought and of the higher emotions. In my opinion, Pavlov laid the foundation of the materialistic [objective] understanding of psychology. The conditional reflexes, as Pavlov put it in a letter to Pierre Janet, seem to exist for all the organs and tissues. The human organism as a whole and all its parts have their representatives in the cortex of the cerebral hemispheres.

The dynamic integrity of the organism may be regarded as wholly corroborated by practical as well as experimental knowledge. Thus began the foundation of a synthetic physiology.

Permit me now to present a rather brief summary of the Pavlovian School of experimental data and after that some facts applicable to neurology and psychiatry.

Due to his extraordinary gifts of observation and experimental skill, Pavlov, as is known, discovered a new class of reflex phenomena arising in the individual's life, hitherto wholly overlooked in experimental practice, a class vast and important, embracing all the reactions of man and animals beginning with the primitive reflex reaction of salivary secretion to the signals of food, including words. Thus every reflex reaction of the brain is a complicated conditional-unconditional reflex, besides those which are formed on the basis of previously originated conditional reflexes, termed by Ivanov-Smolensky conditional-conditional reflexes. These latter may give no external manifestations, and they are revealed intercortically only as a kind of inner speech and those unutterable feelings which are the emotions and "obscure feelings" (Sechenov); they can be connected with the cortico-visceral reactions. The inner cortico-conditional relation is formed by coincidental stimuli in several parts of the cortex and the nearest subcortical centers. According to Pavlov, there occurs a circuit in the cortex of two simultaneously or successively stimulated foci.

At present, by means of electroencephalography, researchers in our country as well as abroad are successful in accurately localising the very area of the circuit of new reflex arcs, in studying the interaction of different points of the cortex as well as of cell groups in separate layers of the cortex and the nearest subcortical structures, including the formatio reticularis.

In the study of intercortical dynamics should be mentioned the researches of Penfield. Even more sensitive are the supersensitive electrical responses of the viscera, revealing the exact locus of excitation and inhibition in the subcortex and cortex, as well as the interactions of the cerebral parts. Pavlov had already described the interaction of cortical foci. Thanks to microelectronics, all these considerations and facts have now been extensively elaborated in the laboratories of Magoun and a number of European researchers (Moruzzi and others). I am hoping that the method of conditional reflexes and electrophysiologic means and devices applied to the study of the dynamics of the cortical processes, will jointly contribute to a deeper insight into the intimate workings of the cerebral nervous elements.

There is now a possibility for utilizing our experimental facts and laboratory observations in the practical work of the neurologists and psychiatrists. The intercortical dynamics in Pavlov's teaching concerning brain function is based on general nervous physiology. As I said before, the conditional reflex arc is formed in the cortex between the afferent centers and the cortical visceral representations. We are not as yet quite sure about the nature of this circuit-mechanism but it is likely to be a summation process arising from repeated stimulations of the same cortical cells and the simultaneous and successive stimulation of the executive effector cells.

When the conditional reflex is elaborated by a definite isolated stimulus, then the excitation extends from the group of cortical cells being immediately stimulated to the neighboring areas due to the irradiation of the excitatory process. During repeated tests the irradiation becomes restricted and the excitatory process is confined to a localised point of the cortex. The restriction of the irradiation-excitation may proceed differently under different conditions, but the chief role is invariably performed by another basic nervous process—the process of inhibition. All the tremendous dynamic system of the cerebral cortex is operated through the interaction of excitation and inhibition. This same interaction forms the basis for the control by the

cortex of all the functions of the living organism. The conditional reflex once formed may exist throughout the life of the organism, or it may on the contrary, disappear. And yet the connection once having taken place, does not completely disappear but is only temporarily suppressed.

Of particular and great importance is the so-called ultramaximal stimulation leading to unconditional inhibition, characteristic of all parts of the nervous system, as opposed to the types of conditional inhibition peculiar only to cortical cells. The ultramaximal or protective inhibition takes place where the stimulation exceeds the working capacity of the given cells. In pathological cells even stimuli of usual strength may evoke an ultramaximal inhibition, which is biologically important for the life of that cell.

Without biological adaptability, all the manifold and harmonious activity of a living organism in all its various interconnections with the external world would be quite impossible.

The cerebral cortex of man and higher animals has the function of reverberating circuits, *i.e.* the function of acquiring, forming, creating new relations between the organism and its environment, the function of developing new life experiences, the function of ontogenetic adaptation.

All these ties between the organism and the environment being strictly determined are secured by the analysis and simultaneous synthesis of that grandiose dynamic system of the billion-cell structure of the cortex, due to the discontinuous flow of stimulation and inhibition, their irradiation and relations of mutual induction.

During the last 20 years together with my numerous and very dear collaborators I have carried out experiments corroborating Pavlov's primary assumptions that it is the cortex that controls all the processes occurring in the human body. Experimental work to that effect, the inferences they led to, and the theoretical formulated conclusions have opened new ways for a study of the normal and pathological functions of the different parts of the nervous system, and for studying the interaction of the subtlest mechanisms of the nervous and humoral factors. We have collected extensive experimental data demonstrating the dominant role of the cortical apparatuses in controlling all the main vital functions. Experimentally we tried to form conditional reflexes through exteroceptors to the activity of the internal organs and the general metabolism. Our colleagues working in clinics were able to observe in their clinical practice, the tremendous role of the cortex in various pathological conditions relating to their emergence, course and recovery. Thus we came to the concept of cortico-visceral physiology and pathology. It appeared that while the cortex affects the internal organs through exteroceptive reflexes, the internal organs of different morphological structure and functional importance, possessing receptor apparatus are themselves, in their own turn, directing signals to the cortex. Thus we managed to elaborate an interoceptor signalization to the cortex. These signals which are formed, on stimulation of mechano-thermo-chemo-osmoreceptors in the visceral receptor fields, enabled us to form interoceptive conditional and unconditional reflexes. The significance of interoceptive signals both normally and pathologically is immense, for the organism is dependent not only upon an appreciation of the external world, but also upon the signals conveyed to the regulatory apparatus, derived from an analysis of processes occurring within the organism itself.

The cortex of the cerebral hemispheres constantly faces two kinds of stimuli : those of the external and those of the internal environment. The wonderful researches on the role of the formatio reticularis are shedding a new light upon the tonic conditions, without which the function of such a complicated dynamic system—as that chief organ of the whole organism's structure, the brain, would hardly be possible.

We admit that Pavlov's teaching concerning the higher nervous activity and its application in psychiatry were not at once adopted by our Soviet psychiatrists. Pavlov himself spoke about it in 1934. He said then that his new ideas on the work of the higher parts of the brain would be accepted only slowly by scientists (psychiatrists and neuropathologists), and that difficulty Pavlov explained as a manifestation of some survivals of dualism—that is of

the age-old habit of separating thought from the brain, of dividing the single and integral human organism into two halves, mind and body. A gradual overcoming of that dualistic outlook contributed to a broader application of Pavlov's teaching to the sphere of psychiatry and neurology. Pavlov's theory does away with all possible dualisms, because the psychic activity is treated by him as a higher nervous activity, *i.e.* as some physiological work of the higher brain, which in principle precludes any contrasting of the psychic and the physiological. Consequently, Pavlov's concept is in its essence one of materialistic monism.

In connection with Pavlov's well known works on schizophrenia, Soviet psychiatrists have made many researches concerning the different forms of schizophrenia (Ivanov-Smolensky, W. P. Protopopov, E. A. Popov). Ivanov-Smolensky in studying the peculiarities of disturbances of the higher nervous activity resulting from catatonia, described two forms of catatonic stupor, one depending upon extensive, and the other upon intensive inhibition. It was he who demonstrated the differences in the higher nervous activity resulting from the catatonic and the paranoiac forms of schizophrenia in different stages of their development and under different conditions of the schizophrenic, and especially in manic-depressives.

A number of research works are devoted to the study of the nervous mechanism of epilepsy and the accompanying pathophysiological alterations of the higher nervous activity (Speransky, A. D., Seredina, and others). One should also mention a series of studies devoted to the pathophysiology of hallucinations and delirium. In our opinion, the most important for psychiatry is Pavlov's concept of "protective inhibition."

Its essence, in brief, may be reduced to the following: if the cortex is affected by some very strong stimuli, there may occur in the cortical nervous cells the so-called transmarginal or ultramaximal inhibition which preserves the cells from exhaustion and destruction. It is this property that Pavlov termed "protective inhibition." The latter may arise in the cells even in reactions to only ordinary stimuli. But they may act not as ordinary, but rather as ultramaximal stimuli, owing to a pathological weakening of the nervous system, such as is not infrequently observed in the first stage of the catatonic form of schizophrenia. Such protective inhibition may take place when the organism is subjected to different intoxications. It may be regarded as a physiological measure of the struggle against injurious influences. But if continued for a long time, such an inhibition may itself prove to be pathological, in which case we witness a shift from physiology to pathology.

On the basis of the concept of protective inhibition a further study of the sleep-cure, started by Pavlov, is being carried out.

Pavlov exerted a considerable influence on psychiatry by his teaching concerning the second signalling system of the cortex. One can say without exaggerating that psychic troubles as a rule result from a disturbance of the second signalling system—the system of speech and thinking. Pavlov used to say: "If you haven't got ideas, you are unable to see facts." His ideas of the second signalling system provide the basis for much new work.

Now let me say a few words about further work on Pavlov's types of nervous system—their relation to the strength of excitation and inhibition, their balance and imbalance, mobility and inertia.

When studying the higher nervous activity we systematically resort to the methods of studying conditional reflexes, EEG, and biochemistry—in particular, the analysis of vitamin metabolism in neurotics. By all these various analyses it was proven that in all the forms of neuroses there is a disorder of the internal cortical inhibition, *i.e.* conditional inhibition, and especially in hysteria.

These data are of vital significance for an understanding of the pathophysiological nature of neuroses in man and their treatment: 1. Treatment with the aid of the so-called (in the USSR) "protective regime," 2. Treatment by means of a protracted sleep, applying minimal doses of soporifics and hypnosis, 3. Training of the inner inhibition, 4. Psychotherapy, hypnotherapy including, 5. Treatment with medicines individually dosed and dependent upon the neurotic type and upon the nature of the disease, 6. Physiotherapy, 7. Medical

physical culture (at the Clinic of Nervous Affections—Prof. Kryshova).

Hypnosis is investigated not only as a phenomenon in itself, but it serves as a method of experimental and physiological analysis of man's higher nervous activity (Physiological Laboratory of Prof. Maiorov), as well as for an analysis of the various hypnotic phases, and the interaction between the first and the second signalling systems.

Pavlov's ideas are gaining ground in the minds of many scientists of other countries. In 1955 there was founded a Pavlovian Society in Baltimore, by Gantt and others.

We do not share Freud's theory of neuroses; it is, in our opinion, devoid of a scientific groundwork. The premise of psychic energy striving for an outlet, and the subdivision of an integrated psyche into 3 parts "Id," "Ego," "Super-Ego" are arbitrary and without scientific confirmation. The dominance of an unrecognizable unconscious in man with his inclinations and instincts is in contradiction to modern neurophysiology and the psychology of man as a social being. Even in the higher animals the acquired conditional reflexes perform an important role. Man's behavior is at the same time almost wholly determined by his social surroundings. According to Freud one of the causes for neurosis is civilisation which restricts instinctive action in man. We hold that certain social environments may be the source of neurosis, not because of restricting instincts, but due to many social contradictions.

One of the main fallacies of Freud's theory is its pansexualism. Far from denying the biologically important significance of the sexual instinct in human life as well as in the origin of several neuroses, we refuse to consider it as the most important factor either in normal life or in pathology. The source of most neuroses is not the mythical Oedipus or the discharge of the suppressed libido, but various external influences, mostly social.

The physiological mechanisms causing neuroses are thoroughly investigated by the Pavlovian school.

Freud's method of psychoanalysis applied to the study of personality is reduced to a sexual interpretation and therefore is tendentious.

The attempts of some researchers, especially in the U. S. A., to combine Freudism with Pavlovian concepts in our opinion lead to no solution whatever. Pavlov himself in general occupied a negative stand to Freud, though he made use of some of Freud's materials to illustrate his own ideas.

Modern psychosomatic medical theory, having enjoyed a particular development in the U. S. A., rests on Freudism and its psychoanalysis and pansexualism. The psychosomatic theory explains the origin of somatic diseases by psychic causes. The cortico-visceral theory also regards the disturbances in the higher nervous activity as a source of a number of somatic diseases. But notwithstanding this seeming likeness, the two theories are directly opposite, the cortico-visceral theory being based on materialistic monism. The organism is an indivisible and integral system, where the cerebral cortex is connected with the internal organs, but the organs are also closely related to their surroundings. The psychosomatic theory is a dualistic one, where the mind is divorced from the body and is only able somehow to affect the latter. The adherents of that theory consider the psychic causes of disease as the unconscious sources of actions and the instincts. Different internal, dermatological and even surgical diseases including traumatic ones, they consider as channels for escape of the unconscious psychic energy.

The psychosomatic theory is widespread in American psychiatry whereas in the USSR it has no place. This is to be explained by our different approaches. In order to attain a common scientific language we should not have to discuss terminology, but we should exert our efforts to a clear understanding of the theoretical foundations of medical science in general and in psychiatry in particular.

An important problem for physiology is collaboration with clinicians. In concluding my talk, I should like to express my desire —that there may be established a friendly working contact with American colleagues, as well as with the scientists of all countries. This would be the best guarantee of the development of that human science, *viz.* medicine, which strives to preserve the health and prolongation of a happy and peaceful life.

THE SIGNIFICANT VARIABLES IN PSYCHOPHARMACEUTIC RESEARCH

LEWIS J. SHERMAN, PH.D.[1]

The literature describing the effects of tranquilizing drugs has reached enormous proportions in recent years(1). Few developments in the history of psychiatry have aroused so much controversy(2) or stimulated so many investigations. Most of the early research gave an unduly optimistic picture of the drugs' efficacy because of inadequate experimental controls and inappropriate procedures(3). Recent studies have shown considerably more methodological sophistication and have placed the value of chemotherapy in proper perspective. It is no longer unusual to find several appropriate control groups, double-blind administrations with placebo, tests of statistical significance, and reliable and quantifiable behavioral measures used in many studies.

Only recently has there been a corresponding increase in our conceptual or theoretical precision to keep pace with this increase in methodological precision(4). Although current studies are now more carefully designed and executed, many significant variables that may influence the drug response still remain uninvestigated and, in some cases, unknown. Undoubtedly the main reason for this situation is the large number of variables relevant to any given problem in chemotherapy research and the difficulties involved in their management. If we intend to gain any valid knowledge of drug effects however, we cannot avoid dealing with these complex forces. By over-simplifying for the purpose of experimentation, we always run the risk of neglecting important influences that will make generalizations beyond the experimental setting impossible. Only by studying many of the important variables—and their various permutations and combinations—can we ever hope to approximate in our research endeavors the complexity of human functioning found in real life.

SIGNIFICANT VARIABLES

A person's response to medication is influenced by the interaction of 3 major classes of variables, namely, drug, situation, and person. All behavior studied in drug experiments, whether measured by rating scales, objective or projective tests, controlled observations, clinical impressions, *etc.*, is some complex function of these 3 variables operating simultaneously upon the patient. Although this conception is generally accepted at a theoretical level (4), it has been frequently ignored when undertaking specific studies. Most investigators have studied only the influence of drug variables and tacitly assumed an invariant response to its pharmacological properties by all people in all places. Fewer investigators have focused on the situation factors that bring about a particular drug effect and, most neglected of all, have been the person variables that determine the uniqueness of each individual's response to the drug. No one has yet attempted to study the effect of all 3 variables within the framework of a single investigation.

The purpose of this paper will be to discuss each of these 3 major categories of variables and to cite illustrative studies of each. An attempt will also be made to outline a methodology whereby all 3 may be investigated simultaneously to determine their joint effect.

DRUG VARIABLES

The overwhelming number of chemotherapy studies are concerned only with the effect of drug variables on behavior. Type of drug, drug combinations, dosage level, and length of administration are the usual dimensions investigated in this category. Situation or person variables are either omitted or presumably controlled by matching groups on several criteria.

In its emphasis on drug variables, the typical chemotherapy study commits the error of oversimplification by assuming that behavior can be isolated from its social context and that the patient is merely a passive recipient of a purely pharmacological agent. It assumes an invariable response

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to the drug: all people reacting in the same way, regardless of the situation in which the drug is administered or the person receiving it. In those studies where no consideration is given to situational or personal factors, authors are forced to state that any improvement in behavior is attributable only to the drug. Such a conclusion has been strongly criticized by Rashkis and Smarr: "It is patently impossible to assume that improvement in patients to whom drugs have been administered is due solely to the drugs themselves"(5). However, the majority of experimenters can reach no other conclusion because of the artificial nature of their research designs.

We have to look no further than to the extremely wide variation in drug results to realize that factors other than the drug are exerting an effect. One review of 52 studies showed 34 to 100% improvement under chlorpromazine and 17 to 100% improvement under reserpine(6). Granting the methodological inadequacies of many of these studies, it is clear that the drug alone is contributing only a portion to the total effect and that other factors—equal, and in some cases more important—must be operating to influence behavior.

SITUATION VARIABLES

It has long been recognized that the psycho-social environment in which the patient resides and receives treatment has a determining effect on his behavior. The findings of Stanton and Schwartz(7) that staff harmony and discord may be reflected in patient functioning, the conclusions of Greenblatt, York, and Brown(8) that patients may improve without any formal therapy simply by being in a "therapeutic milieu," and Caudill's recent work(9) on the total hospital atmosphere all support this thesis. It is evident that patients are not treated in a vacuum and that they respond to a variety of subtle forces around them in addition to the specific therapeutic agent under investigation.

Those social forces impinging upon the patient from the research and hospital setting and those psychological influences stemming from the various personnel with whom he comes in contact are the situation variables that must be considered in psychopharmaceutic research.[2]

It is necessary to specify the total social situation in which any drug experiment is carried out. No comparisons between separate studies or replications of single studies can be made without a clear description of the research context. A recent report(10) emphasizes this precaution and as a guide to such description lists 19 items, under the general headings of Hospital Structure, Hospital Personnel, and Patient Population, which may have an influence on patient response. Size, location, architectural characteristics of the hospital; number, training, description of personnel; and special characteristics of the patient population are some of the variables considered important in this regard. It is also recommended that ". . . any alterations in the setting introduced by the investigator or by circumstances after the study was begun" should be clearly specified because of the possible influence they may have on behavior. The importance of this latter point is documented in a study by Wing (11) which used a sociologist as ward observer. He found the observer's presence on the ward crucial enough to bring about an initial improvement in patient behavior, and this improvement was later reversed when the observer was no longer unfamiliar to the patients.

In spite of the multiplicity of significant variables operative in the social setting, only the research unit specifically has received much attention. That improvement in behavior can occur solely by being selected as a subject and by residing on a research ward has been clearly demonstrated by Rashkis and Smarr(5). Forty-eight chronic female schizophrenics were observed on a research unit for 7 months prior to the administration of drugs in order to establish a pre-drug base line. Thirty-nine of these 48 showed improvement without medication due to what the authors term a "milieu effect" and even after 7

[2] It is recognized that the distinction between social and psychological situation variables is artificial. For example, the psychological attitudes of ward personnel are very closely related to the social philosophy of the hospital. However, the distinction will be made for purposes of exposition and to categorize the several relevant studies concerned with these variables.

months many had not yet stabilized. This finding is an illustration of the "Hawthorne Effect"(12) originally observed in industrial settings over 20 years ago where increased attention, heightened interest, and social stimulation alone were responsible for changes in behavior.

Gerard considers these "milieu effects" of major significance and primarily responsible for the enthusiastic early reports on the effectiveness of tranquilizers :

> I think it has been demonstrated sufficiently that, at least in the earlier stages of drug testing, those hospitals which were reported to get the greatest change with the introduction of tranquilizers were the ones that had almost a completely custodial attitude. Prior to the drug experiments, the patients had been pretty much neglected ; now they were given attention as well as a drug(13).

A comprehensive study now under way is attempting to assess directly the influence of the total social setting on drug response (14). The cooperating hospitals are the very large acute and custodial Boston State and Metropolitan State Hospitals and the "130-bed Massachusetts Mental Health Center which is an active treatment hospital with a multi-discipline approach to therapy and rehabilitation." The specific aims of the study are to determine the differing effectiveness of drug therapy between large state hospitals and a small intensive treatment center. By transferring selected patients from one study hospital to the other, the investigators can see whether social therapy alone is superior to drug therapy alone or whether social and drug therapy together is more beneficial than either one separately.

Recently, some attention has been devoted to the second group of situation variables, *viz.*, the psychological influences stemming from personnel attitudes and feelings. Quite early in the development of the tranquilizers it was noted by the staff of the Michael Reese Hospital that they were not obtaining the same degree of improvement with drug therapy as workers in other hospitals(15). This led them to study the attitudes of their personnel toward drugs as a possible determining factor in their lower improvement rate. After an intensive qualitative analysis of the hospital setting, they concluded that attitudinal factors were indeed important and that contributing to their lack of success was ". . . the relatively negative attitude of our hospital personnel toward the prescription of drugs as compared with alternative modes of therapy"(15).

A quantitative study by Feldman(16) on the relation of staff attitudes to treatment outcome agrees with the above findings. He found a high relationship between the attitudes toward drugs of 37 physicians and their success with the drugs. Those physicians most enthusiastic about medication and convinced of its value had by far the greatest patient improvement. One investigator, for example, who was completely sold on the merits of tranquilizers had 77% of his patients improve ; another who considered drug therapy "contrary to our dynamic concepts" and a waste of time had only 10% improvement. Related findings by Thorpe and Baker(17) have shown that nurses' attitudes toward medication are also of importance and influence their judgments of patient improvement.

In view of these few, but nevertheless highly suggestive, findings that ". . . there is a significant relationship between the enthusiasm of the investigator and the therapeutic effect of the drugs"(1), it seems evident that more research efforts should be directed at this problem. The typical drug study, which only states that certain physicians, nurses, and aides attended the patients during the course of the study—but says nothing of their beliefs and feelings about drug therapy—seemingly ignores a relevant research variable.[3]

PERSON VARIABLES

The most neglected area in chemotherapy research has been the relationship between drug effects and the personality of the drug recipient, *i.e.*, the influence of person variables on behavior. While it is a truism that "people are different," apparently many in-

[3] Research in this area has been facilitated by the construction of an objective scale to measure attitudes toward tranquilizing drugs by Mason and Sacks(18). Although primarily devised for use with physicians, it can be modified to apply to nurses and aides as well. Attitude scores have shown a significant correlation with actual use of drugs by physicians and are now being correlated with several measures of patient improvement.

vestigators have assumed that (a) these individual differences will balance out in their experimental designs and contribute equally to all groups, or (b) that drugs exert an invariant effect regardless of the personality differences of the people receiving them. The few studies that have concerned themselves with the problem of individual differences show that neither of these assumptions is necessarily true.

The considerable literature on placebo effects(19, 20), although not usually concerned with tranquilizing drugs, nevertheless has relevance here. The several studies by Lasagna, Beecher, and von Felsinger (21, 22, 23) have all demonstrated that "the nature of the subject" is an important determinant of drug effects. It appears that there are discernible personality characteristics which account for a certain portion of the effect of any given drug. One study on the influence of morphine and a placebo on pain reduction showed that 42% reported some relief of pain following the placebo injection. From a psychological test battery, the authors were then able to characterize these "placebo reactors" in terms of some specific personality patterns(24).

Confirming these findings are the investigations of Hill(25) and Kornetsky(26) wherein objective measures of personality functioning were used. In many cases they found that personality differences brought about behavior which minimized and even went contrary to the typical physiological effect of the drug. There were indications that a "general drug sensitivity" factor exists in some people which causes them to react to all drugs. Other subjects not possessing this factor are less affected by drugs. Relatively little is currently known about the personality variables underlying these idiosyncratic reaction patterns. In summarizing his work, Kornetsky is insistent on the importance of person variables in drug research :

> The effects of drugs on psychological performance in man are due not only to the specific pharmacological activity of the drug, but also to the specific reactivity of the subject and to an interaction of the two(26).

It is unfortunate that the rarest type of objective chemotherapy experiment is the one that would answer the most important question facing the psychiatrist : Will this drug benefit this *particular* patient with his unique background, motivation for treatment, personality structure, and symptoms ? The few tranquilizer studies that have investigated this problem of individual differences suggest there is a relationship between the nature of the drug recipient and his drug response. Ellsworth and Clark(27) were able to relate improvement under reserpine and chlorpromazine to a patient's variability in pre-drug "palmar sweat ratings" or generalized anxiety level. Kornetsky and Humphries(28) found high correlations between MMPI psychasthenia and depression scores and their patients' subjective and objective behavior changes following the administration of several drugs. Finally, Kelly *et al.*(29) correlated 68 individual personality variables with the behavioral effects of meprobamate and proclorperazine. Although many of the significant correlations obtained may be due to chance because of the enormous number tested, the investigators still feel that, "Each significant correlation has interest as a potentially fruitful hypothesis for future experimentation"(29).

The final group of studies investigating the determining role of personality are those conducted within a dynamic or psychoanalytic framework. They attempt to explain the divergent chemotherapy results in terms of the individual's psychological perception of the drug and what medication means to him. Epitomizing this approach is the comment by Fernandes that

> the effect of the (tranquilizing) drug upon the whole personality is salutary or detrimental, according to the way it is experienced by the patient's ego, and the way it is elaborated and valued by the patient himself(30).

Sarwer-Foner, in a series of related investigations, has similarly emphasized that

> The therapeutic effect (of drugs) . . . is due not to the pharmacological action alone, but to the way in which this physiological action psychologically influences the patient's defences in terms of the patient's total situation(31).

In the course of evaluating 5 different tranquilizers, Sarwer-Foner found clear-cut untoward reactions in about 17% of his

cases. These patients, instead of showing behavioral improvement, developed panic and paranoid reactions, agitation, increased withdrawal, and enhanced anxiety. He offers as hypotheses for these negative reactions the psychological meaning the patient attributed to the physiological effect of the drug. For example, those patients who typically use motor activity as the main defense against unconscious passivity may become threatened and anxious by the drug's restraining action. Similarly, those patients with strong latent homosexual conflicts may interpret the administration of the drug as "an unwelcome assault or seduction" and react adversely to the chemotherapy. Although these studies have been criticized by Bennett(32) for their methodological shortcomings, they stand as significant exploratory works which can furnish hypotheses for more precise experimentation. There is too little known about the relevant personality variables operating in the psychopharmaceutic situation to discount any possible sources of influence in our research designs.

FACTORIAL DESIGN

It has been shown that a patient's response to medication is influenced by the interaction of drug, person, and situation variables. Changes in behavior are due not only to the type and quantity of drug administered but also to the total social setting in which treatment occurs, the feelings and attitudes of personnel attending the patient, and the personality structure of the drug recipient. Studies which investigate only one or two of these influences can furnish only partial answers to our research questions. It is clear that what is needed is a research design that will permit the simultaneous study of several of these variables in a single experiment.

Such a procedure is called a factorial design.[4] "A factorial design is one in which we have two or more variables each varied in two or more ways and studied in all possible combinations"(33). In contrast to the traditional approach of holding all but one variable constant, in a factorial design the experimenter deliberately varies as many factors as he is interested in studying. This procedure is more comprehensive than other methods because interactions between variables as well as the main effect of each variable may then be studied. It is also more economical because a wide range of conditions are sampled using fewer subjects and observations than would be required in conducting separate studies for each factor.

In brief, a factorial design can answer more than one question in a single experiment. It can tell us not only that one drug is superior to another, but also under which treatment conditions and for which types of patients this superiority obtains. This latter information is of primary importance in drug experimentation. Edwards and Cronbach stress the necessity of going beyond a simple "A better than B" approach in evaluative research :

> It seems obvious at this point that simple comparisons of (Drug A and Drug B) may often be relatively worthless, and that comparisons gain value as the design isolates the specific types of persons and situations for which A is superior(33).

A single factorial experiment could study the relative effect of each of the 3 major classes of variables outlined in this paper. For example, we could investigate within the framework of a single study the changes in behavior produced by Drugs A and B (drug variables) in chronic and acute schizophrenics (person variables) when treatment occurs in custodial and rehabilitative hospitals (situation variables). The several questions asked in this research are each answered by an analysis of all the possible main and interaction effects.[5] From the wealth of information that could possibly be obtained from

[4] An excellent account of the research possibilities of factorial design is contained in the article by Edwards and Cronbach(33). Although concerned specifically with psychotherapy research, it is also applicable to chemotherapy research. More technical discussions may be found in McNemar(34), Kogan (35), and Edwards(36).

[5] Main effects are the ones that occur consistently regardless of variation in any other experimental factors. For example, one drug may be superior to the other irrespective of the types of patients or the hospital setting. Interaction effects are the ones due to a combination of two or more experimental factors. For example, one drug may be superior to the other *only* when administered to particular types of patients or *only* when given in a particular hospital setting.

such a study, the basic advantage of a factorial approach is clear : *the more variables systematically investigated, the more comprehensive the information obtained.*

In view of the considerable evidence that changes in behavior are not merely a function of the drug itself, it is surprising that so many studies still neglect or attempt to hold constant all other relevant variables. Instead of excluding these non-drug sources of influence, we should recognize their existence and, by using a factorial approach, actually build them into our research designs. Only in this way can the combined influence on behavior of drug, situation, and person variables ever be ascertained and more valid knowledge of drug effects obtained.

SUMMARY

This paper has reviewed selected studies that indicate the importance of situational and personal factors on a patient's response to drug therapy. A factorial research design has been proposed as the appropriate means of evaluating several of these significant variables in a single experimental study.

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HELLER'S DISEASE AND CHILDHOOD SCHIZOPHRENIA

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The problem of differentiating psychogenic from organic symptoms is often a challenging one, and this applies in particular to the field of child psychiatry. In discussing the severe personality deviations of pre-school children, under the title of "atypical development," Rank(1) stated:

> By this term we refer to those severe disturbances in early development which have been variously diagnosed as Heller's disease, childhood psychosis, childhood schizophrenia, autism, or mental defect.

Such indiscriminate grouping of etiologically different conditions can however be misleading both for theoretical and practical reasons.

Since so-called Heller's disease is most apt to be confused with childhood schizophrenia, it is proposed here to delineate the former condition and to illustrate the problem of differential diagnosis from schizophrenia through a clinicopathologic analysis of a series of cases.

Under the designation of dementia infantilis, Theodor Heller(2) described a disorder in 28 children whom he observed and followed between 1905 and 1930. According to Heller, these are children who, without preceding illness, become conspicuous in their third or fourth year of life through symptoms of a character disorder. Whereas they have been placid or lively by nature until that time, they become moody, negativistic, disobedient, often raging without reason, or whining. They tend to be destructive, and many show anxiety states, occasionally of an hallucinatory character. Following these initial symptoms, they rapidly undergo a process of mental regression which leads within a few months to a complete loss of speech and to apparent idiocy. During the regressive period, motor disturbances frequently become evident. The children acquire tic-like movements, they grimace and pose in peculiar positions. Many become incontinent of urine and sometimes also of feces. It becomes necessary to feed them. During all of this, there remains a certain degree of attentiveness, yet they are unresponsive to any approach through remedial education.

Heller was of the opinion that this condition did not belong to the group of schizophrenias. However, according to Kanner (3), it was customary to list Heller's disease among the varieties of infantile schizophrenia until Corberi found in brain biopsies performed on 4 such patients "diffuse lipoid degeneration of the ganglion cells." These findings led to the assumption that the condition represented a cerebral degenerative process akin to Tay Sachs' disease. Since, however, blindness was not a feature of the disorder, it suggested a process similar to that described by Kufs and by Walter as "amaurotic idiocy without amaurosis." Kanner could find no case reports of Heller's disease in the American literature and stated:

> I have seen only three unequivocal cases. In one it was possible to obtain specimens of brain tissue through a biopsy done in Dr. Walter Dandy's department. Evidence of widespread cell degeneration, especially in two layers of the cortex, was unmistakable.

He also refers to reports by Kennedy and Hill, and by Jancke, of Heller's disease following pertussis. Kanner emphasized the essentially organic basis of Heller's disease as distinct from the condition of infantile autism which he first described and which he regarded as fundamentally schizophrenic in nature.

CASE REPORTS

The cases to be described consisted of 3 separate pairs of siblings and are therefore considered below under their respective family names.

Family R.—Lynn, a 15-year-old girl, developed normally until the age of 3 years when she began to exhibit increasing difficulty in walking and irregular twisting movements

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of the arms and body. At the age of 6, her speech became slow and indistinct. When she started school, she became a behaviour problem. For example, she would go to the boys' toilet and expose herself, would tell many fantastic tales and her school work was poor.

At the age of 10, she was examined in a pediatric outpatient clinic, at which time she exhibited flight of ideas and inappropriate emotional reactions. There were mild neurologic signs consisting of dysarthria, choreoathetoid movements of the hands and arms, ataxia on finger to nose and heel to knee tests, a somewhat unsteady broad-based gait, hyperactive deep reflexes and questionable pallor of the temporal half of the left disc. An EEG showed evidence of generalized dysrhythmia. Laboratory tests, including examination of the spinal fluid, were negative. A diagnosis of mild athetoid form of cerebral palsy was made but, because of the prominence of the psychiatric features, she was admitted for further observation to the psychiatric clinic where she remained for approximately a year.

In the hospital, the patient was first described as dishevelled in appearance, preoccupied, varying in mood between unmotivated, mirthless laughter and apparent sadness, and incoherent in her conversation. She appeared to respond to auditory and visual hallucinations, for example she talked about seeing little objects walking around in the air. It was difficult to test her sensorium. Her behaviour was erratic, impulsive and often violent. Psychologic tests led to the conclusion by the psychologist that "from the nature and severity of this girl's personality disturbance, it seems possible that this factor alone could account for the disturbed intellectual functioning." The psychiatrist felt that there were sufficient psychogenic factors in the girl's environment, such as parental discord, to account for an emotional disturbance, quite apart from any organic factors. The final diagnoses were juvenile schizophrenia and athetoid form of cerebral palsy. During the course of her hospitalization, the patient was said to improve inasmuch as she became less destructive, and appeared more responsive. She was taken out of the hospital against advice and remained at home. Her further course was one of steady decline, so that in the last 2 years of her life, she became completely unable to walk or talk. Death occurred at the age of 15.

Roger, younger brother of Lynn, now aged 14 years, was said to be well until about the age of 12, when he began showing tremor of his hands and personality changes. From a quiet good student he became very talkative, neglectful of his personal appearance and failing in his school work. More recently he has been hallucinating, believing that termites were crawling in his bed and complaining that people were persecuting him and going to hang him. He was afraid to leave his mother's side even for a moment and preferred to remain alone and daydream.

Examination in the pediatric clinic revealed nystagmus, ataxia and athetosis. On the Wechsler-Intelligence scale for children he was awarded a full scale I.Q. of 68 but the psychologist remarked that "the record was not unlike that of a schizophrenic process-confused, perseverative and evidencing residual learning." The results of the Bender-Gestalt test also suggested a psychosis. An EEG was considered as moderately abnormal. Laboratory tests, including examination of the spinal fluid, were negative.

When last seen, the patient was showing signs of further deterioration.

Family E.—Marilyn, a 7-year-old girl had a normal birth and early development. At the age of 3 years, she was said to have been frightened at a Halloween party. The next day she appeared fearful and began nocturnal screaming, which continued unabated for the next 6 weeks. She gradually became more seclusive, negativistic and mute, was unable to adjust in kindergarten, and later developed incontinence of urine and feces. At the age of 5, she was examined in the pediatric clinic. Physical examination was negative and there was no mention of any neurologic abnormalities. The psychologist described her as showing "essentially marked instability in her emotional reactions, varying between lethargy, unmotivated laughing and crying, and between mutism and outbursts of unintelligible words and songs." She was awarded an I.Q. of 33, on the Kuhlmann-Stanford and of 47 on the social maturity test and was committed to a hospital for the mentally retarded where she continued to deteriorate until her death at the age of 7.

JoAnn, younger sister of Marilyn, developed normally until the age of 5, when she began to exhibit awkwardness, speech defect, spells of trembling and retardation in her school work. When examined in the pediatric clinic at the age of 7, she showed ataxia, dysarthria, mental regression and EEG evidence of paroxysmal dysrhythmia. She continued to deteriorate and, by the age of 9, her I.Q. was estimated at 55 and a few months later at 30. The further outcome of her case is at present unknown.

POSTMORTEM FINDINGS

The significant pathologic findings in the two patients who died were limited to the central nervous system. In each case there was widespread disease of the neurons, from the cerebral cortex to the spinal cord. The changes consisted of ballooning of the nerve cells, their dendrites and axons, as a result of deposits of a lipid material. This consisted of granules which stained poorly with the scarlet red method for neutral fat but positively with the Nile blue sulfate method, for fatty acids and other more complex lipids. (Fig. 1a, b, c, d.)

COMMENT

It was obvious that the diagnosis in the above cases was amaurotic family idiocy. In the absence of amaurosis it appeared to be a form of the disease, previously referred to as "amaurotic idiocy without amaurosis." Its onset at the age of 3 years in the two cases that died suggested the Bielschowsky-Jansky or late infantile form of the cerebral lipoidoses. In the experience of the author, such cases are not uncommon, but in the absence of the specific retinal findings, are often misdiagnosed. It is noteworthy that in the still living siblings the correct diagnosis was made only after the autopsy in the two patients who died revealed the true nature of the disease.

Family M.—Sharon, a 13-year-old girl, had a normal birth and early development. When she started school at the age of 6, it was noted that she was slow in comprehension, repeated grades and had to be placed in a special class. At the age of 8, her behaviour became bizarre and impulsive, and she was observed to have "blank spells." When examined at a local hospital, an I.Q. of 62 was determined and diagnoses of mental deficiency and petit mal epilepsy were considered. At the age of 11 she was hospitalized for a year in a children's psychiatric clinic. Some of the examiners characterized her behaviour as autistic with diminished speech, punctuated by irrelevant and bizarre responses, mannerisms, and sudden shifts of mood from fearfulness to apathy. Others described her speech as dysarthric and her movements as choreiform. The psychologist concluded that she was showing "classical schizophrenic signs with perseveration of movement, speech and ideation, tics, grimaces and mannerisms, clinging physically to adults with increased motility and reduced verbalization." An EEG disclosed a slow disorganized record with evidence of generalized paroxysmal dysrhythmia. Her final diagnosis was established as childhood schizophrenia with catatonic features. She continued to deteriorate and was transferred to a State hospital for the mentally retarded where her condition was diagnosed as degenerative chorea. She died there at the age of 13 years.

Ronald, aged 11 years, younger brother of Sharon, developed normally until about the age of 5-6 years. When he started school, he did poorly, was considered emotionally disturbed, requiring placement in a special class. At the age of 8, he was referred to a mental hygiene clinic. There, he was described as hyperactive, fearful, having a short attention span and his I.Q. was determined at 54. He was diagnosed as mental deficiency with schizophrenic reactions. At the age of 10 he was admitted to the same psychiatric clinic as his sister. Like her, he was variously described as excitable, confused and erratic or as undergoing abrupt involuntary choreoathetoid movements. The psychologist felt that "the patient demonstrated signs of deterioration which were either on a schizophrenic or organic basis." The patient was committed to a State hospital where his EEG was described as a slow, disorganized record with a spike and wave activity suggestive of convulsive susceptibility. He died there at the age of 11 years.

POSTMORTEM FINDINGS

The pathologic findings in the two siblings of Family M. disclosed changes in the brain of an unusual type and location. They were degenerative lesions that involved symmetrically and severely the corpus Luysi and to a lesser degree the mammillary body and the mammillo-thalamic tract. In these areas, the neurons and their nerve fibers had virtually disappeared, leaving only a few shrunken nerve cells and fibers behind, accompanied by a dense reactive fibrillary gliosis. (Fig. 2a, b, c, d.)

COMMENT

The lesions in the two cases bore the stamp of a primary degenerative disease because of their absolute restriction to these two nuclear masses and because of their symmetry. This was further confirmed by the identity of the changes in the two siblings indicating the heredofamilial basis of the disorder. In the experience of the writer, such a disease with pathoanatomic

confirmation has not hitherto been reported in the literature. From the standpoint of the clinical picture it is reasonable to assume that the involuntary choreiform movements and the dysarthric speech could be attributed to the lesions in the corpus Luysi. For, as is well known, this nucleus is a component part of the extrapyramidal system, disease of which has often been associated with such disturbances of movement as ballismus. Whether the hyperkinesia in these two children was one of ballismus or chorea remains undetermined perhaps because attention was focused on the psychiatric picture and as a result the neurologic status was not carefully evaluated. The clinical manifestations of the lesions in the mammillary bodies are not as obvious. However, these may be compared with such other disorders in which the mammillary bodies are primarily affected as for example Korsakoff's syndrome. In all such instances it is possible that disturbances in emotional expression and other psychic functions can be attributed to a disruption in the connections of the limbic system of which the mammillary bodies form a link.

Discussion

The cases reported above illustrate several types of organic brain disease occurring in childhood, in which the clinical manifestations were those of progressive psychologic and neurologic deterioration. As such they closely resembled the cases described by Heller, even though such a diagnosis was not actually made. It is apparent, however, both from the present cases and others from the literature that the designation of Heller's disease is not sufficiently precise, can in fact be misleading and therefore should be abandoned. For not only has it become a waste basket diagnosis for all sorts of organic brain disease but, more important, it has been confused with childhood schizophrenia.

In agreement with Kanner, the aim in diagnosis should be to distinguish between disease entities along etiologic lines. In our cases, the familial occurrence and the postmortem findings clearly established the hereditary metabolic or degenerative nature of the disease in each of the cases. However, the familial trends and the precise diagnosis were not established until after the pathologic findings were determined in each one member of a pair of siblings.

Retrospectively, the diagnosis of childhood schizophrenia appeared to have been made by either ignoring or underestimating the role of the organic factors in the total picture. For example, the motor disturbances, such as the choreiform movements, were considered to be tics or mannerisms, and the abnormal EEG findings were not taken into consideration. Instead, the emotional and behavioural disturbances became the focal points of interest. Even when the organic factors were recognized it was felt that the personality disturbances were on a different basis. Their etiology was searched for and discovered in certain traumatizing environmental or psychogenic factors. In the opinion of the writer it does not appear that there was sufficient proof for the latter contention. Rather, the "schizophrenic" symptoms in the cases seemed to be directly related to the brain damage. As already stated previously, Kanner was convinced of such an interpretation of the syndrome of Heller's disease. It should be emphasized that the term schizophrenia, when applied to such cases as are here discussed, is misleading since it fails to recognize the specific metabolic nature of the disease in question and consequently directs interpretation of the condition and treatment in a wrong direction.

Summary

1. Six cases of children with organic brain disease, which were clinically diagnosed as childhood schizophrenia, are analyzed clinicopathologically.

2. The diagnosis of Heller's disease or of childhood schizophrenia, often made under such circumstances, is considered respectively inadequate and misleading.

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THE ADMINISTRATION OF BAS, 5-HTP, AND MARSILID TO SCHIZOPHRENIC PATIENTS

AARON FELDSTEIN, HARRY FREEMAN, JUSTIN M. HOPE, IRIS M. DIBNER AND HUDSON HOAGLAND [1]

Woolley and Shaw(1, 2) first proposed early in 1954 that a deficiency or excess of serotonin in the brain might be a cause of schizophrenia. To test the hypothesis, Woolley(3, 4) suggested that 5-hydroxytryptophane (5-HTP), the precursor of serotonin, be administered to schizophrenic patients. If serotonin had no relationship to schizophrenia, then the patients should not react. On the other hand, if the disease were caused by a deficiency of serotonin, then 5-HTP should have a therapeutic effect and if the disease were caused by an excess of serotonin, then 5-HTP should intensify the schizophrenic symptoms. 5-HTP was suggested rather than serotonin itself since serotonin does not readily cross the blood-brain barrier, whereas 5-HTP does. We wish to report on the clinical and biochemical effects of 5-HTP administered to 5 chronic schizophrenic patients. At Woolley's suggestion, 1-benzyl-2, 5-dimethylserotonin (BAS) was preadministered in order to protect the patient against the gastrointestinal effects of excess serotonin (4). Two of the patients received Marsilid in addition to the BAS and 5-HTP to inhibit the presumed monoamine oxidase destruction of brain serotonin.[2]

In the first study, 4 male chronic schizophrenic patients were selected from the research ward of the Worcester State Hospital. The first week served as a control period. During the second and third weeks, each of the patients received orally two 50 mg. tablets of BAS daily. During the fourth and fifth weeks the administration of BAS was continued and the patients received in addition an intramuscular injection of 15 mg. of 5-HTP twice daily. The sixth week served as a control period.

In the second study, using the same patients but one, the dose of 5-HTP was increased from 30 to 100 mg. a day. One of the patients (BER), was dropped and another male patient (YAN) substituted. The first week served as a control period. During the second, third, fourth and fifth weeks, 50 mg. tablets of BAS were given orally twice daily to each patient. Two of the patients (CAR and AKE) in addition to the BAS received 50 mg. of 5-HTP, i.m. twice daily, throughout the third, fourth and fifth weeks. The other two patients (BEN and YAN) in addition to the BAS received 50 mg. of 5-HTP, i.m. and 50 mg. of Marsilid, orally, twice daily, throughout the third, fourth and fifth weeks. The sixth week of the study served as a control.

The schizophrenic patients showed no change in behavior; the psychiatric clinical picture was completely negative in all 5 patients. BAS alone, BAS combined with 5-HTP, and BAS and 5-HTP in conjunction with Marsilid were of no therapeutic value. Rudy and coworkers(5) studied 24 moderately disturbed psychotic females; they reported that BAS exerted predominantly a tranquilizing action and that 20 of the patients improved at maximum dose. Woolley (4) reported on 12 schizophrenic patients that had been treated with combined BAS and 5-HTP; he noted that only 3 of them showed an immediate improvement, but this was not sustained. He concluded that this treatment did not alleviate the disease. Our findings agree with those of Woolley.

The administration of Marsilid which may be expected to increase the brain serotonin levels over that expected from the use of BAS and 5-HTP failed to alter the negative clinical picture. While only 5 chronic cases are represented in this study the evidence casts doubt on the hypothesis that too little or too much serotonin *per se* is causally related to schizophrenia.

[1] The Worcester Foundation for Experimental Biology, Shrewsbury, Mass., and The Worcester State Hospital, Worcester, Mass.

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Urines were collected systematically throughout the studies at about 10 A.M. after discarding the waking samples. The urines were analyzed for 5-hydroxyindoleacetic acid (5-HIAA) by the colorimetric method of Udenfriend(6) and chromatographed in a two-dimensional system(7), spotting 200 ul. of urine and spraying with Udenfriend's reagent to detect 5-hydroxyindoles and with Ehrlich's reagent to detect other indoles.

The expected increase in urinary excretion of 5-HIAA following the administration of BAS and 5-HTP combined was not observed even at a dosage of 100 mg./day of 5-HTP for 3 weeks (Table 1). Only one of the patients (BER) showed an increase and this accounted for only 40% of the 30 mg. of DL-5-HTP injected (calculated on the basis of the L-form only). The administration of BAS by itself caused no change in the urinary 5-HIAA excretion pattern of the schizophrenic patients. There are two possible explanations for these facts: 1. That schizophrenic patients lack one or more of the necessary enzymes to convert 5-HTP to 5-HIAA and 2. That BAS alone causes a metabolic block. We have presented evidence(8) that the urinary levels of 5-HIAA and the blood levels of serotonin are not significantly different in schizophrenic patients and normal subjects, which would suggest that the enzymes necessary for the conversion of 5-HTP to 5-HIAA are present and operative in schizophrenic patients as well as in normal subjects. It may be concluded that BAS blocks the conversion of 5-HTP to 5-HIAA. The fact that BAS and Marsilid prevented the formation of 5-HIAA from 5-HTP is not surprising since Marsilid is an inhibitor of monoamine oxidase.

The paper chromatograms clearly showed the presence of the 3 major 5-hydroxyindoles, 5-HIAA, serotonin, and 5-HTP after the administration of 5-HTP to the schizophrenic patients pretreated with BAS. The spots due to serotonin and 5-HTP were not observed in the control period or after the administration of BAS alone. The accumulation of serotonin in the urine strongly suggests that BAS is a monoamine oxidase inhibitor. This is consistent with the findings of Woolley and Edelman(9) that mice treated with BAS showed no increase in urinary 5-HIAA, but that urinary serotonin was markedly increased. It is interesting to note that although both BAS and Marsilid are monoamine oxidase inhibitors, BAS acts as a tranquilizer and Marsilid acts as a psychoenergizer. This suggests that the energizing property of Marsilid may not be a function of its ability to inhibit monoamine oxidase. The accumulation of 5-HTP in the urine may be due to the specificity of the decarboxylase for the L-form with the resultant accumulation of the D-form. The Marsilid and non-Marsilid chromatograms were qualitatively the same with respect to the 5-hydroxyindoles.

An antidiuretic effect was observed in only 2 patients (CAR and BEN), (Table 1) after the administration of 30 mg./day but not after 100 mg./day of 5-HTP. There was as a result a concomitant increase in the concentration of 5-HIAA; the output of 5-HIAA when calculated on a time basis however showed no change due to administered 5-HTP in these 2 patients.

TABLE 1

THE URINARY EXCRETION OF 5-HIAA AFTER INTRAMUSCULAR ADMINISTRATION OF 5-HTP TO MALE CHRONIC SCHIZOPHRENIC PATIENTS PRETREATED WITH 100 MG./DAY OF BAS ADMINISTERED ORALLY

Patient	Administered 5-HTP (mg./day)	Output of 5-HIAA (μg./ml.) BAS Alone	5-HTP + BAS	Effect[b] of 5-HTP	Output of 5-HIAA (μg./hr.) BAS Alone	5-HTP + BAS	Effect of 5-HTP	Output of Urine (ml./hr.) BAS Alone	5-HTP + BAS	Effect[b] of 5-HTP
BER	30	8.8	24.6	inc.	162	433	inc.	18.1	21.5	—
CAR	30	8.8	13.4	inc.	638	584	—	77.0	26.8	dec.
	100	5.6	9.5	—	412	462	—	78.3	63.8	—
AKF	30	8.0	7.4	—	420	533	—	68.5	75.1	—
	100	4.2	9.2	—	454	338	—	92.2	41.7	—
BEN	30	8.5	16.4	inc.	317	405	—	39.1	24.8	dec.
	100[a]	6.5	10.4	—	192	200	—	34.7	20.4	—
YAN	100[a]	4.0	5.5	—	329	312	—	77.2	59.6	—

[a] In addition to 100 mg./day of BAS and 100 mg./day of 5-HTP, these patients received 100 mg./day of Marsilid.
[b] Where an increase or decrease is indicated, statistical analysis indicates $P < .01$.

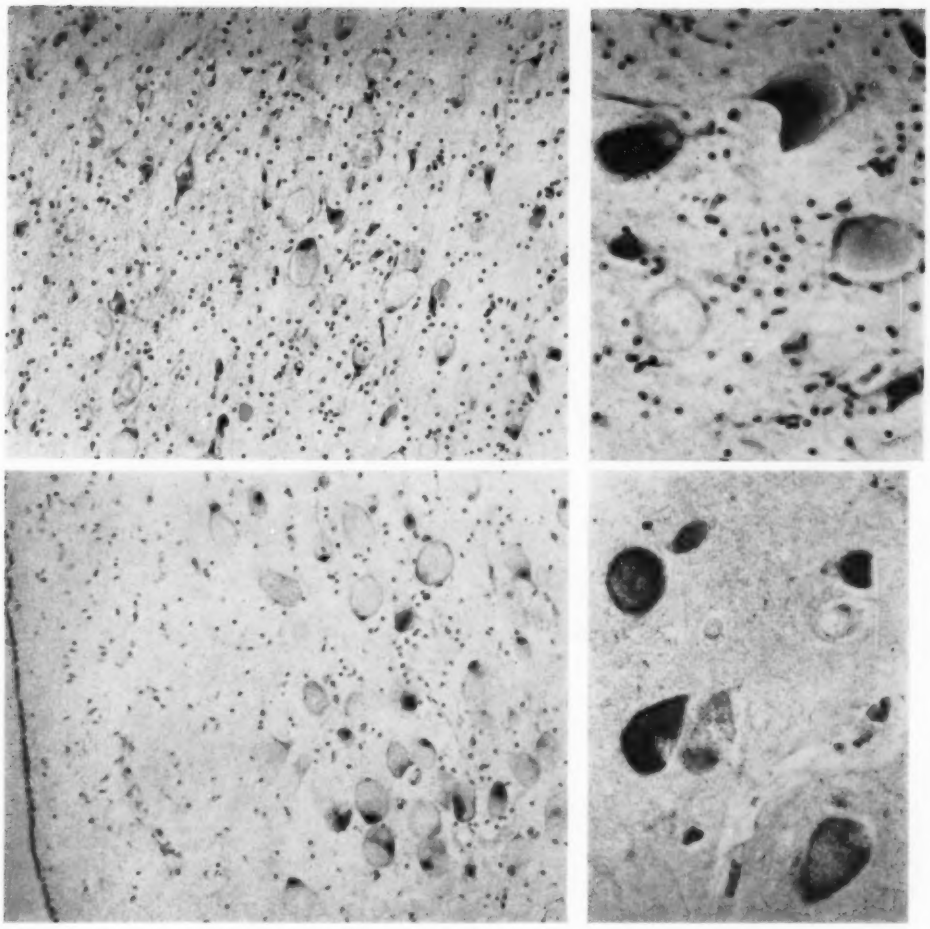


FIG. 1

Ballooning of neurons of (a) corpus Luysi, Nissl stain x 105 and (b) anterior horn cells of spinal cord, Nissl stain x 345 ; Case L.R. (c) Same changes in paraventricular nucleus, Nissl stain x 105 and (d) deposits within the neurons of granular lipid material staining deep blue with Nile blue sulfate method x 475 ; Case M.E.

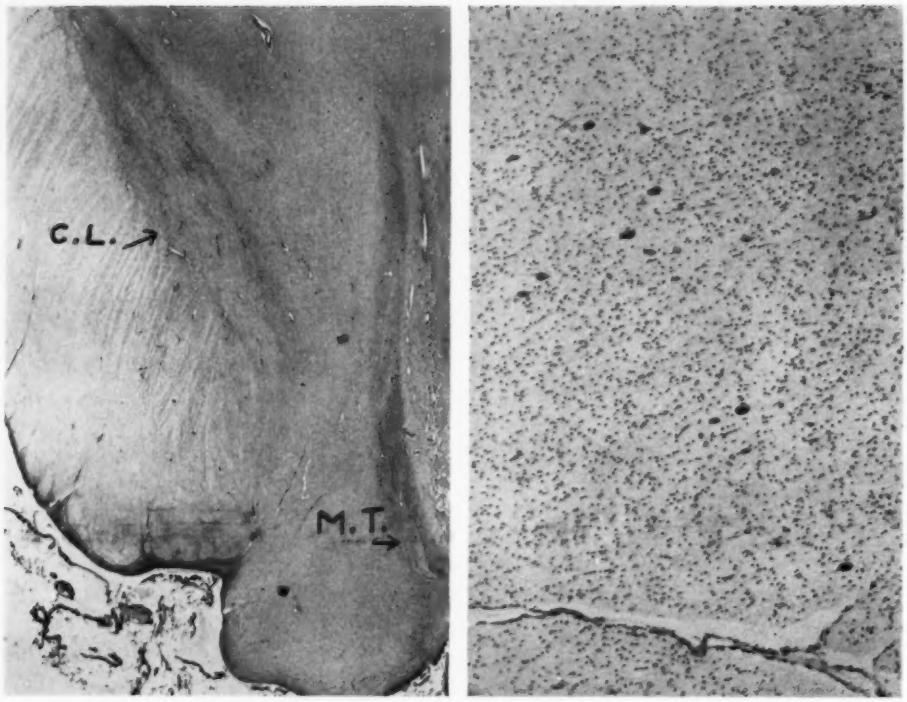


FIG. 2 A AND B

Chronic degeneration as evidenced in (a) by gliosis of corpus Luysi (C.L.) and mammillothalamic tract (M.T.), Holzer stain x 10 and in (b) by paucity of neurons and reactive proliferation of glial elements in the corpus Luysi, Nissl stain x 100 ; Case of R.M.

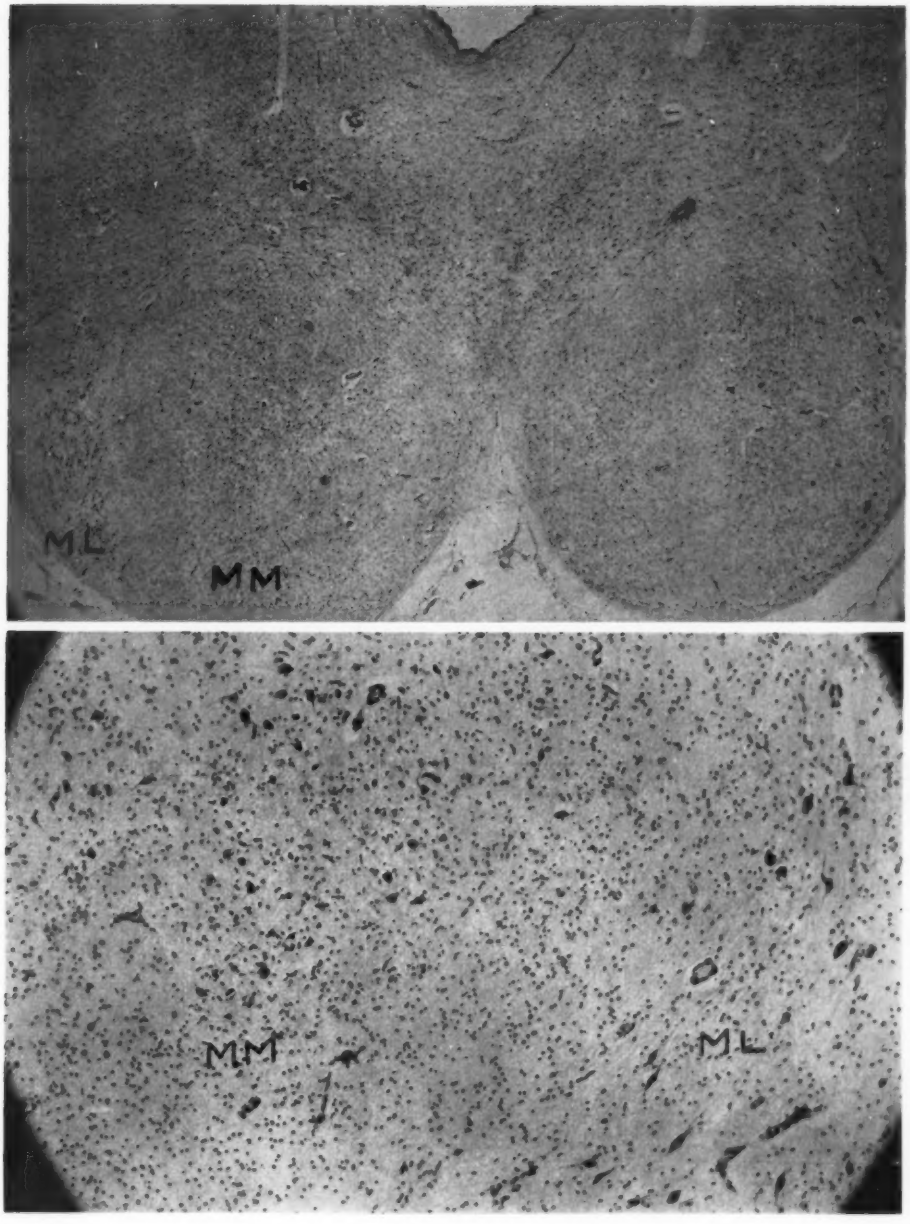


FIG. 2 C AND D

Chronic degeneration, characterized by disappearance of neurons from the medial mammillary nucleus (MM) by contrast with normal appearance of lateral mammillary nucleus (ML) in (c) Nissl stain x 21 and (d) Nissl stain x 110; Case of S.M.

SUMMARY

The administration to 5 chronic schizophrenic patients of BAS alone, of BAS and 5-HTP combined, and of BAS and 5-HTP in conjunction with Marsilid was not therapeutically useful. The fact that the patients did not react to the presumed increase in brain serotonin casts doubt upon the hypothesis that too little or too much serotonin is causally related to schizophrenia.

BAS appears to be a monoamine oxidase inhibitor. The conversion of 5-HTP to 5-HIAA was thus prevented resulting in an accumulation of serotonin in urine.

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THE ROLE OF PREFRONTAL LOBE SURGERY AS A MEANS OF ERADICATING INTRACTABLE ANXIETY

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Let us establish promptly the fact that this study, in contradistinction to most reports on the results of psychosurgery in literally hundreds of patients, concerns itself with the selection, and post-operative results obtained in only 18 patients. However, they are 18 consecutive patients, spread over a period of 10 years and painstakingly selected because their presenting symptoms, their underlying personality traits and their intense degree of intrapsychic distress made us all feel that prefrontal surgery had an excellent chance of success. In no case was surgery decided upon as a "last resort" procedure, nor was it used in any of these patients simply to make them easier to take care of and less of a nursing problem. In the selection of patients for surgery the diagnostic classification was largely ignored and this small group includes nearly every non-organic category except mental deficiency and psychopathy.

The common denominator in all members of this group and the sole reason for surgery, was the presence of severe, long-standing anxiety and agitation, repeatedly resistant to the usual therapeutic approaches and disabling to the point that the patients could no longer carry on their business, marital or social existence. Five of our 18 were patients who had been obviously psychotic and had been hospitalized for many years prior to surgery. They were operated for the same intensely distressful symptoms as the non-psychotic group. All 5 are still hospital residents but the emotionally unbearable tensions for which surgery was done, have been removed in 3 and alleviated in 2. Of the 13 patients who managed to maintain their grip on reality in spite of such disabling factors as uncontrollable gross tremors, intense insomnia and recourse to heavy barbiturate and alcohol dosage, 12 have left the hospital and have been able to resume their normal existence with no further hospitalization or treatment indicated, for periods ranging from 6 months to 8 years, with the post-operative followup averaging 4 years.

This series of consecutive cases is taken from the files of a small, private mental hospital where maximum individual attention can be given to each case. The patient census is seldom over 40, and with 3 full-time psychiatrists, it is obvious that one will have the great advantage of scores of hours spent at individual interviews. It is believed that the success of this series has been largely due to the resultant careful selection of candidates for surgery and a clear aim established for each one prior to operation. The ability to concentrate on the evaluation and investigation of an individual patient has caused us to decide against surgery in at least 50 patients initially considered for it during the years that this group was selected. In the evaluation of each case the only factors considered in the initial decision are the degree of anxiety and its duration. The history usually shows that this has been present for several years and under ordinary circumstances has been attacked vigorously by various means. Frequently the patients have become dependent upon barbiturates or alcohol in an attempt to alleviate their suffering. Usually large amounts of these agents have produced only slight diminution in their symptoms. In our group of 18, all were treated with ECT either prior to admission, or by ourselves, or both, but it has been our experience that even those reactions primarily characterized by depression will gradually build up a threshold of resistance to repeated series of ECT, while those patients who possess a considerable component of anxiety and agitation tend to do poorly with ECT from the start.

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It must be emphasized that the decision to utilize frontal lobe surgery was reached in every case only after we became convinced that other forms of treatment had failed. The tabulation of individual patients shows that the duration of study and continuous treatment leading up to surgery averaged 14 months, not including the psychotic, chronically hospitalized group. All of them had received adequate electroshock without permanent benefit; some had received entirely too much, considering its repeatedly demonstrated inability to control anxiety in each particular case. All were the recipients of literally scores of hours spent in supportive therapeutic sessions, often during periods of persistent insomnia in the hours after midnight if it appeared that a therapeutic "breakthrough" could be hoped for at such a time. All were at the same time subject to physiotherapy, hydrotherapy, occupational and planned recreational therapy as well as the usual battery of drugs, both tranquilizing and directly sedative. In the majority of the non-psychotic group we also utilized an average of 8-10 lengthy interviews at night under intravenous amytal, not only to promote abreaction and subsequent sleep but to help in uncovering any strongly hostile, paranoid or antisocial *anlage* that would militate against the use of surgery, due to its tendency to release temporary aggression. If all of these approaches resulted in no consistent relief for the patient and all of the exploratory probing with Rorschach, TAT, Bellevue-Wechsler, amytal and daily clinical contact turned up no serious contraindication, we still set up one last hurdle to overcome before discussing surgical therapy with the patient or relatives. In recognition of the fact that surgery constitutes an irreversible approach to this problem, and to guard against our own increasing enthusiasm because of some very favorable early results, we decided in 1952 to request independent consultation from a source unconnected with Craig House to interview and study the patient separately, arrive at a decision for or against surgery before group conference with us. For maximum benefit to the patient, the consultant should preferably be one whose background, training and discipline would probably influence him away from surgery. We asked Dr. Lawrence Kubie to consult with us under the above circumstances and he has examined many of the patients since 1952 that are included in this study. Several others do not appear here because we did not always reach unanimous agreement and they were not operated. This process of elimination was our last self-imposed road block in trying to avoid error in selection of candidates and it probably represents one of the main reasons why almost 95% of our small, non-psychotic group have returned home to a normal life and stayed there, the first ones operated now having remained out of hospital 6, 7 and 8 years without the necessity of further therapy.

Throughout the 20 years since Moniz first reported his work in 1936, the one consistent result of frontal lobe surgery seems to have been the reduction or relief of intra-psychic tension. For the most part, lobotomies of whatever depth or extent have been directed at the amelioration of the severely disturbed behavior of the advanced schizophrenic, with the relief of tension largely an interesting but incidental minor note. However, for our purposes it is the most important result of what is now a very modified, less extensive procedure, because in all of these 18 patients the sole aim of surgery was to give the patient relief from severely disabling anxiety and break up the concomitant tension. A 60-year-old man, hospitalized for the first time, who has had only 6 hours sleep in a week, sitting slumped in a chair with his teeth constantly chattering, muscles twitching and eyes dilated, totally unable to concentrate, is just as disabled as a hebephrenic praecox who doesn't even know you are in the room. In fact, he is even more pitiable because only 6 months ago he was an active vice president in a large investment house in New York. He still has the intellectual potential but now the selection of a necktie presents an insoluble problem and he can only pace the room with pointless activity and chattering teeth. Repeated series of ECT, Thorazine and barbiturates couldn't touch him, intravenous amytal at night would give 45 minutes anesthesia, to be followed by re-

sumption of panic. Another male patient, age 46, and with 20 years successful business life behind him, locks himself in his stateroom and slides the key under the door to his wife during a cruise because when on deck there is an uncontrollable impulse to jump overboard. He comes to us after years of repeated hospitalizations, ECT, and insulin coma, and his "solution" for the control of the intense compulsive-obsessive neurosis has been to hole up in various small hotels away from home, to drink himself into an anesthetic state alone for days on end with complete loss of self-respect. These are the types of problems that constitute this list of patients. After a variable number of months or years in spite of all efforts of their own and their physicians, they have arrived at an impasse in which they are chronically miserable, no longer able to support themselves, manage a home or even live up to ordinary daily responsibilities. The referring physician has done his best to maintain an attitude of optimism but he has "tried everything," and eventually recommends another hospitalization and probably more electroshock because he is well aware that the patient's gradual disintegration of personality, coupled with a growing aura of quiet desperation, has all the necessary ingredients for self-destruction. All of these patients in the Acute Group, without exception, had very seriously considered suicide at some point in the progress of their illness as the only remaining escape from the torment of uncontrollable anxiety, agitation and fear. The possibility that surgery might offer a reasonable and safe solution of this dilemma almost never occurred to the harassed referring physician for the simple reason that the great majority of physicians, including our own specialty, have written off frontal lobe surgery as a therapeutic weapon for any illness short of chronic major psychosis. The type of patients necessarily selected from the big state hospitals for the early work in this field and the emotional flattening resulting from the wide, deep and extensive cuts originally employed, have set up a mental image of the lobotomized patient that it will take many years to erase, through current surgical progress and perhaps studies such as this. It is significant of the general attitude that only one paper on frontal lobe surgery was scheduled at San Francisco for last year's APA meeting. Of this group of 13 who eventually came to either topectomy or pre-coronal leucotomy, 11 came to us with the expressed hope on the part of the referring physician that by the act of hospitalization and the further use of electroshock and tranquilizers we could somehow hold the line against progressive disintegration and self-destruction, surgery not even being considered. The remaining 2 patients were sent in specifically to determine the potential value of leucotomy for them as individuals. This proportion reflects the attitude of most psychiatrists.

In the non-psychotic group there are certain criteria that must be met by the patient. The first and most important of these is the history of an adequate premorbid personality. There must be evidence that the patient was able to live constructively with his neurosis and make an acceptable emotional adjustment before the intractable anxiety and agitation began to tear down his defences. We know definitely that topectomy and pre-coronal leucotomy will remove the anxiety but if there has never been a solid level to which to return it is doubtful if surgery is justified. Second, if extensive clinical and psychological investigation indicates an appreciable tendency toward paranoid formulations, or the possible release of aggressive and destructive behavior we have not risked surgery except in one patient. Admittedly, this restriction may have been too conservative, since in Great Britain there are now upwards of 20,000 post-operative leucotomies, and investigators of the stature of Sargant and Maclay have expressed the opinion that this danger is probably overestimated, particularly in the less extensive undercutting utilized here(9). A third important consideration to evaluate before surgery is the probable emotional atmosphere to which the patient will return after hospitalization. The attitude of the patient's spouse is particularly crucial since marital discord can occur when the returned patient, demonstrating much less dependency that during the months or years prior to surgery, threatens

the security of an authoritarian or immature spouse. In this small group we have had one divorce, another threatened divorce and a third situation, wherein the patient, freed of anxiety but showing no other personality change, had to "take over" as head of the family when her husband could no longer dominate her and himself retreated into a regressive neurotic pattern of behavior.

The importance of frequent educational contact with families is one of the reasons why we have practically demanded that patients remain in the hospital for at least 60 days after surgery. Of more direct importance to the patient is the fact that this period is felt to be very crucial to the eventual outcome. The convalescent weeks are divided roughly into thirds. During the first 3 weeks the patient will be quite slothful, will sleep a good deal to make up for lost sleep and exhaustion, will be hedonistic, humorous, probably sarcastic and quite tactless in conversation and relationships with others. The only limitations imposed are that he must stay on the hospital grounds, must have a nurse with him at all times and not engage in any activity such as heavy exercise or swimming that might endanger his post-operative physical status. He eats and sleeps when he pleases and is encouraged to behave in any manner he desires, within obvious limitations. After one month the night nurse is removed and pressure is gradually exerted to get him organized into a pattern of regularity in his sleeping, meal hours, hygienic routine, proper selection of clothes and the observation of good general manners and courtesy towards others. Usually this routine is established after about 6 weeks but we have found that if a patient is at home and continues to do as he pleases it may never be established. During the last 2 weeks the patient is usually put on his own responsibility, the day nurse is removed, he begins to go home for week-ends and plans for his future are discussed with him for the first time. Not until the last few days do we discuss his past illness, the reasons for surgery, or attempt to determine changes in his mental content following surgery. In general the patient is more than pleased to concentrate on the present and future and expresses himself as "well rid of the past." Dilantin is continued for one year after surgery combined with ascorbic acid to prevent gingivitis.

Certain results have appeared so consistently in these patients that we feel they should be noted even though the small number of cases makes any statistical approach valueless.

1. With the surgical removal of pathological states of anxiety and tension there seems to be immediate cessation of the need for barbiturates and alcohol. It was the usual sequence of events that patients who had been unable to sleep at all without heavy sedation, and slept poorly even when heavily sedated, would sleep soundly on the night following operation and thereafter without hypnotics. The same general observation was also true of the daylight hours, wherein prior to surgery these patients kept up a constant pressure to obtain any drug, including alcohol, that would promote peace of mind through suppression of frontal lobe activity. We have not operated in any case to specifically influence this type of addiction but it might have much to offer.

2. We found, as have many others including Freeman, Sargant and Scoville (10), some remarkable somatic changes in those conditions known to be influenced by emotional tension. One patient, age 54, had been hospitalized 4 times for severe, bleeding ulcerative colitis, was maintained on a very restrictive bland diet and was told at her last hospitalization, 2 months before psychiatric admission, that her only chance of recovery was through colectomy. During the first week after topectomy, uninhibited by dietary restrictions she literally gorged herself on fresh corn, cauliflower, high residue salads, celery *etc.* stating in high good humor "even if it kills me it's worth it." She had no unfavorable reaction, has now been eating whatever she wants for 4 years and has had no further diarrhea, bleeding or other symptoms of colitis to present writing. One of us (J. L. P.) has a very similar case in his own series in whom ulcerative colitis was repeatedly demonstrated by sigmoidoscopy prior to leucotomy. She is now about 8 years post-op, has been clinically recovered since surgery

and routine proctoscopic and sigmoidoscopic examination demonstrated the rapid return to normalcy of the intestinal mucosa. Three of these patients, plagued for years with hay fever and asthma in June and September, noted a marked improvement in their allergies. Another patient, a 30-year-old paranoid schizophrenic, had truly emaciated himself and developed active, far advanced tuberculosis through refusal to eat. He had been given a total of 110 electroshock treatments in trying to combat this and on admission he still consistently refused food. Topectomy in this case was definitely a gamble but he has not missed a meal in 5¼ years, his tuberculosis is entirely arrested and, although still a schizophrenic he is able to spend increasing numbers of weeks at home because he is greatly improved in health, mood and behavior. Only 3 of our patients were hypertensive but they showed a gratifying initial drop in pressure for several months, thereafter have gradually risen but are still not up to pre-operative levels. Nearly all of the patients seemed to drop years of age in their facial expression and appearance, with the ironing out of lines of fatigue and tension as well as a change of facial expression away from a chronically worried and haggard appearance. This was frequently brought to our attention by the visiting families, or the patients themselves.

3. Apparently no group of patients are as grateful to their physicians as those who have had relief of symptoms through frontal lobe surgery. Ordinary process of follow up seems largely unnecessary with this group because about 90% either write to us regularly, telephone or report back to the hospital from as far away as Texas and Arkansas. Questionnaires always get a total response and several patients have spontaneously volunteered to talk to prospective surgical candidates if they were fearful or hesitant about having surgery done. This was never necessary because once a patient surmounted the initial shock of contemplating brain surgery and could be actually promised relief he usually tried to advance the date of operation stating, "I would rather be dead than the way I am now." We consider this continued friendliness and desire to maintain contact long after leaving the hospital to be a most gratifying result of the procedure. The well-known habit of the former patient snubbing his psychiatrist in public does not seem to prevail here. Perhaps this pleasant reversal of form has increased our enthusiasm for this therapeutic procedure.

A few brief observations are in order concerning the technical aspects of surgical treatment. They are contributed by our surgical co-author and are based on the follow-up of approximately 500 of his own post-operative cases, inclusive of this small group. Perusal of long-term follow up reports suggests that the surgical *placement* of frontal lobe lesions is important, whether it be by cortical ablation as in topectomy(3), or by disconnection of the thalamo-hypothalamic frontal white fibers as in lobotomy(4). Both topectomy and lobotomy studies indicate that best results with minimal intellectual or emotional deficit follow bimedial subfrontal operations (5) rather than operations on the lateral or superior aspects of the frontal lobe(8). It has also been established that the quantity of surgical removal or disconnection is significant(6). Too little proves therapeutically ineffective, while too much impairs the functional capacity of the brain. Another factor that must be weighed in gauging the surgical extent of these procedures is the degree of any existing brain pathology that may be encountered at operation, such as atrophy, discoloration, undue firmness of the convolutions, a milky arachnoid membrane or advanced arteriosclerosis(3)(6). Such findings, also noted by others(7) in about half the brains so visualized, may lead one to more conservative surgery than otherwise, since some degree of brain damage already exists. While the microscope fails to indicate the nature of these changes(8), they are grossly sufficiently prominent and prevalent to make one wonder about the possibility of metabolic, biochemical or other organic disease of the brain as the cause of the emotional disturbance in at least some of these cases.

Topectomy, a topical resection of a block of frontal lobe cortex(8), of proven value in its day, has now been discarded because it involves a longer and far more arduous

operative procedure than lobotomy, without achieving superior therapeutic results. In lobotomy, operative fatalities have been reduced from 3% to zero and no longer do urinary or fecal incontinence, postoperative hemorrhage, lasting euphoria or flatness of affect occur unless these conditions existed prior to surgery.

Summary

A series of 18 consecutive patients were selected for frontal lobe surgery over a 10 year period to obtain relief from chronic, intractable anxiety. Of the 13 who were not psychotic, 12 have returned to a well adjusted, independent existence at home without further hospitalization or continuation of therapy. Certain observations based on these case studies have been made, with full realization that generalizations cannot be drawn from 18 cases and that whatever value this study may have is dependent upon intense personal investigation of all relevant factors in a small group of individuals.

Conclusions

1. Topectomy, or more recently modified leucotomy, is the treatment of choice for severe anxiety states that have proven resistant and intractable. Surgery offers, in our opinion, a far better chance of relief from the intense and disabling symptoms of guilt, self-recrimination, anxiety and the disorganizing effect of repetitive, uncontrollable patterns of obsessive thought than does any other form of therapy presently available.

2. It is not presumed that the operative procedure is in any way curative of the underlying personality disturbance that is creating intensely distressing symptoms but it relieves the suffering of the patient in a manner that appears prompt, predictable and permanent.

3. The procedure is safe. In the hands of a skilled and experienced neuro-surgeon there have been no fatalities and a carefully planned bimedial prefrontal lobotomy appears to carry little risk of rendering a patient worse in any way. In only one of this group of 18 cases has there been any undesirable side-effect. This patient had been actively psychotic and continously hospitalized for 18 years, requiring extensive, bilateral removal of tissue by topectomy in order to accomplish the relief of severe somatic delusions. During the 6 years followup she has had 3 grand mal seizures in spite of anticonvulsants but it has been a small price to pay for the relief of symptoms obtained. This complication represents 5.5% of the total series.

4. Based on long term clinical observation and psychological testing after surgery there has been no evidence of intellectual impairment, defects in concentration, retention or memory. In fact, the contrary has been repeatedly noted by patients and families as well as business associates. They report an alertness, organization and ability to concentrate that usually has not been present in that specific patient for months, sometimes years, prior to operation. The patients themselves explain this by the fact that their minds, free of self-recrimination, anxiety and fear, can return to normal function. One male patient, now almost 2 years post-operative, returned to full duty as chief auditor of a large industrial establishment 2 months after operation and is currently writing a highly technical textbook on cost accounting. One of us, (J. L. P.) has a private series of cases exclusive of this group, which consists of 27 men and women who today, 10 years after topectomy or lobotomy operation, are conducting a full and normal life and are responsible for committee work, business mergers *etc.*, so successfully that no one is aware of the fact that brain surgery has been done.

5. Careful selection of cases and prompt surgery before there is any deterioration of personality, or before excessive ECT creates an "electrical leucotomy," have been found to yield the best results.

6. The procedure has at least humanitarian value in providing relief from unbearable tensions in severely psychotic patients suffering from persistent somatic delusions.

7. The possibilities inherent in this safe procedure for the treatment of such conditions as severe ulcerative colitis, anorexia nervosa and even constantly recurrent peptic ulcers have not yet been even superficially explored in this country. Given any

choice, the authors feel that they would much rather undergo both the surgery and the aftermath of pre-coronal leucotomy than colectomy or gastrectomy, to say nothing of retaining an intact gastro-intestinal system.

8. In view of the duration of symptomatic relief in these patients it seems reasonable to hope that the results achieved may be permanent.

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TABLE 1

Chronically Ill—Still Hospitalized

NAME	*Age & Sex*	*Duration Illness Years*	*Previous Hospitalizations*	*E C T*	*Pre-operative Study*	*Diagnosis*	*Disposition*	*Years Follow-up*	*Remarks*
C. D.	63 Male	20	2	2 series 30 Insulin & metrazol 30	24 mo.	Involutional Agitated depression severe	Still in hospital but agitation and anxiety almost absent	11	Goes home frequently, jovial, excellent sense of humor
P. B.	61 Female	12	2	2 series 18	6 mo.	Psychosis, type undetermined, severe agitation	Remains psychotic but definitely improved in anxiety and agitation	7	First leucotomy insufficient, bitemporal done 1952
C. C.	49 Female	18	4	3 series 38 Amytal 12	30 mo.	Schizophrenia, paranoid	Makes excellent adjustment for weeks outside of hospital	6	Surgery done to stop intense agitation due to bizarre somatic delusions. Excellent result
W. M.	30 Male	3	5	5 series 110 Insulin Coma 120	4 mo.	Schizophrenia, paranoid	Discharged to open service at another hospital. Long visits home	5½	Admitted with far advanced bilateral T. B. Refusal of food. Wt. 86 lbs. Operated to break up rapid downhill course. Gained 50 lbs. T. B. arrested
S. L.	33 F	7	1	1 series 11	48 mo.	Schizophrenia, hebephrenic	Operated to lessen intense fear due to bizarre visual, auditory & somatic hallucinations	2½	Basic illness unchanged, but much less tortured, more content, severe agitation eliminated

TABLE 2

NON-PSYCHOTIC—ACUTE GROUP

NAME	Age & Sex	Duration Illness Years	Previous Hospitalizations	E C T	Pre-operative Study	Diagnosis	Disposition	Years Follow-up	Remarks
B. W.	55-F	3	1	2 series 26	10 mo.	Agitated depression	Home—full recovery. No further treatment	8	Fully managing own home
I. E.	36-F	12	3	2 series 13	21 mo.	Compulsive-obsessive Severe	Home—full social recovery	7	No further treatment
D. E.	63-M	4	6	3 series 23	5 mo.	Agitated depression	Return to full business & social responsibilities	6	Remarried without recurrence
E. Y.	56-F	2	3	2 series 25	9 mo.	Agitated depression	Returned to normal life	5½	No further treatment
E. K.	66-F	3	2	1 series 6	3 mo.	Reactive depression—marked anxiety	Returned home to manage own business affairs	5	No further treatment
G. D.	47-M	14	4	2 series 23 Insulin 40	3 mo.	Compulsive-obsessive Severe	Discharged to manage own factory and drill oil wells	4½	Writes frequently. No recurrence
E. K.	50-F	22	11	3 series 38	38 mo. repeated hosp.	Manic-depressive, mixed	Home—no further attacks	4½	Longest period remission by far
M. H.	54-F	½	0	2 series 10	3 mo.	Agitated depression	Resumed very active & responsible home life	4	Recovery also from severe ulcerative colitis
P. T.	33-F	4	2	3 series 46	12 mo.	Manic-depressive. Marked agitation	Levelled off since surgery. No further cyclic attacks	4	Marked improvement but apathetic
J. K.	46-M	1½	4	1 series 16	13 mo.	Compulsive-obsessive Intense anxiety	Return to full duty as top actuary in large industry	1½	Apparently, full recovery
C. W.	65-M	7	5	4 series 38	1 mo.	Agitated depression with organic features	Discharged home—very much improved	1	Died of coronary—1 year post-op.
M. E.	65-F	5	3	3 series 20	4 mo.	Agitated depression	Discharged—still active & doing well	1	Unusually independent post-op.
N. R.	55-F	6	4	2 series 24	60 mo. Outpatient	Agitated depression Intense anxiety	Home to resume full social & domestic duty	5 mo.	Abrupt change in personality—no residual anxiety

CRITERIA FOR THE SELECTION OF A SMALL GROUP OF CHRONIC SCHIZOPHRENIC SUBJECTS FOR BIOLOGICAL STUDIES:

Special Reference to Psychological (Family Unit) Studies

SEYMOUR PERLIN, M.D.[1] AND A. RUSSELL LEE, M.D.[2]

A review of the literature reveals little attention to the problem of the selection of schizophrenic subjects for biological studies(1, 2). In the published history of such research, the explicit theory or method underlying patient selection is rarely noted. Further, an analysis of the implied process indicates avoidance of such issues as the feasibility of random sampling, non-purposive sample bias, the range of variation with respect to such irrelevant and complicating conditions as age and hospitalization, and the means by which subjects may be duplicated in a pertinent manner.

A major area of interest of the Laboratory of Clinical Science at the National Institute of Mental Health lies in the application of the biological sciences to the problem of mental disease. A long-range multidisciplinary program of studies in the biological aspects of schizophrenia is currently in progress(3). For this purpose, a limited number of beds are available.

Since any program involving intensive psychological and biological studies will be limited with respect to the number of patients, the theory and process of the selection of the sample assumes considerable importance. So far as we know, no attempt has been made to bias a sample for biological studies in the manner to be presented.

It was felt at the outset that any sample chosen should reduce to a minimum those variables which are not characteristic of, or clearly relevant to, schizophrenia (in order to reduce the likelihood of false positives) and maximize the likelihood of inclusion within the sample of those forms of schizophrenia (if they exist) in which biological abnormality plays a significant role. Further, appropriate criteria of selection once established could provide a basis for duplication and extension of particular findings in a larger group.[3]

RESTRICTION OF VARIABLES

This method of screening chronic schizophrenic subjects for biological studies presumes that chronic schizophrenia is a continuing psychophysiological process. (No assumption is made as to the possible modification of causal factors during the course of the disease.)

However, even if schizophrenia reflects a psychophysiological state, the latter may not be manifest except under certain conditions of stress. For example, the schizophrenic may compensate psychophysiologically in such a way as to be indistinguishable from normal-controls; on the other hand, the schizophrenic may also decompensate under a stress such as criticism and may only then reveal an aberrant psychophysiological condition.

It is possible that the manifestation of chronic schizophrenia may be caused primarily by such social forces as hospitalization, in contrast to the manifestation of acute schizophrenia which may reflect an underlying physiological disorder. These considerations suggest the alternative and

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perhaps preferable screening of acutely disturbed students or military personnel and also childhood schizophrenics in future biological studies.

Restriction of the following variables is especially important since, under the conditions noted, they may be irrelevant to schizophrenia.

1. *Age*—A number of biological function patterns have been best described for normal subjects between 20 and 35 years of age. This suggests a comparable age range for patient selection. Below 20, biological patterns are apt to show the marked variation characteristic of the adolescent period. The upper limit of age 35 excludes a population in which aging is an important variable.

2. *Sex*—Male patients are preferable for the following reasons: (a) Many more "normal" biological values are already established for males. (b) The psychophysiologic phenomena of menstruation are avoided. (c) Dependable urine collection is more feasible in males.

3. *Race*—The possibility of pertinent and significant racial differences cannot be rejected *a priori*. Since most control studies have been done in white populations, and since the white schizophrenic group is larger and better characterized, purposive selection is easier in this group.

4. *Length of hospitalization*—The period suggested is between 3 and 5 years. On an initial screening, length of hospitalization is thought to be a more meaningful criterion than duration of illness because of the difficulty in evaluating historical data available at the time of a screening procedure. The minimum figure of 3 years hospitalization is in accord with data indicating that once a patient has spent 3 years in a hospital, his chance of being discharged is significantly decreased(4). This means that the group is more likely to be available for long-term biological studies and to fulfill, to a greater degree, those requirements for the diagnosis of schizophrenia based on prognosis. The maximum of 5 years is chosen in an attempt to limit the more extreme effects of long hospitalization. Within such a group, evaluations of psychophysiological compensation or decompensation may be utilized as criteria for further selection(5, 6).

As noted, the acceptance of these limits implies the need for other samples or comparison groups comprised of acute schizophrenic patients who have not been hospitalized or who have been hospitalized for less than 3 years.

5. *Freedom from overt complicating factors*—Medical evaluation done as part of the screening process must maintain focus on factors related to both patient status and hospitalization which will alter related biological studies. For example, "training status"(7), which reflects the activity or inactivity of the individual should be considered in addition to nutritional status. Individual differences as well as the effects of hospitalization must be evaluated. Data regarding the administration of vitamins and antibiotics should also be noted. Many patients hospitalized for this period of time will have had insulin, electroconvulsive and psychopharmacological therapy. The amount of treatment given and any complications of therapy should be considered in selecting cases.

A DESIGN FOR SELECTION: A BIASED SAMPLE

Concepts of randomness and bias as applied to the selection of schizophrenic subjects.

Random sampling is frequently emphasized in the literature. In many projects, however, the randomness is clearly not within the total population of schizophrenic patients, but rather within a heavily biased subgroup which will vary from study to study. On one level this may represent the bias of a "random cooperative" sample, where cooperation is needed for collection of specimens, *etc.* Cooperativeness, in turn, may be highly correlated with a chronic versus acute subsample or with a paranoid versus a hebephrenic subsample. Many samples seem especially weighted by cooperative, chronic, paranoid patients.

Frequent biases for the selection of schizophrenic subjects are: patient cooperation, activity level, psychodynamics, subtype, symptoms, level of compensation, ability to have behavior recorded and

potential for a control.[4] Such stratification results in subgroups within which random sampling can *then* be done. Our goal is not to sample a chronic schizophrenic population randomly but rather to bias our selection with reference to the biological studies.

An operational framework for considering organic versus environmental factors in schizophrenia and its relevance to the biased sample.

For purposes of discussion, we may consider schizophrenia as a continuum of disease, at one end of which the etiology is organic and at the other, environmental. Organic and/or environmental factors may be involved in the expression of the disease as well. If schizophrenia consists of multiple entities, however, these same assumptions, for purposes of discussion, would hold for each entity or syndrome. Our purpose here is not to defend one point of view against another, but rather to indicate the consequence of such points of view in our operational approach.

We may examine this approach in terms of each of the following alternative postulates:

1. The primary etiology of schizophrenia is environmental: there are no *relevant* organic factors.

2. There are organic factors, but these are secondary to the environmental. (a.) Such organic factors are necessarily present. (b.) Such organic factors are variably present.

3. The primary etiology of schizophrenia is a single organic factor: there are no *relevant* environmental variables.

4. Organic and environmental factors are simultaneously etiological and relevant.

5. There are multiple entities within the "group of schizophrenias." For each entity 1, 2, 3 or 4 may hold.

These postulates should not be considered as composing in their totality a theoretical model of the etiology of schizophrenia; only those postulates are noted which would basically alter our screening procedure. (Concepts regarding the persistence or sufficiency of these factors in the expression of schizophrenia may modify but will not be crucial in determining selection strategy.)

If the primary etiology of schizophrenia is environmental and there are no relevant organic factors, (postulate 1), no method of selection will increase the probability of finding significant biological variables. If the primary etiology is a single organic factor and there are no relevant environmental variables, (postulate 3), then the significant defect will be revealed by the appropriate biological test in *any* selection of schizophrenics. Under such circumstances, the randomness and the size of the sample are unimportant. Thus, the biasing process, however incorrect in theory or application cannot exclude the desired subjects, *i.e.*, those who would reveal the significant defect.

The necessary or variable aspect of biological findings, secondary to environmental causes (postulate 2) is not distinguished in our working design. Similarly, organic and environmental factors which are simultaneously etiological and relevant (postulate 4) are not distinguished in this approach. Hopefully the *number* of variable aspects may be reduced by restricting irrelevant variables in selection as well as in the management and evaluation of the experimental population; contributory information may be obtained through the use of ward observations, ratings of affective states, serial testing, *etc.*, and in the concurrent evaluation of both the experimental schizophrenic sample and a contemplated normal-control sample(8).

Our working hypothesis assumes that there are multiple entities within schizophrenia or within the group of schizophrenias, (postulate 5); this is the least restricting assumption for our selection strategy. Only if important organic defects are inconstant, will the selection process affect the probability of their discovery; it is therefore on the basis of this postulate that the present theory of selection has been developed. Following from this, we seek to bias our selection in favor of the biological types of schizophrenia.

Process schizophrenia as the basis of a

[4] See Perlin, S.: Geriatrics, 13: 747, Nov. 1958, for illustrations of non-purposive and purposive bias in the process of selection.

biased sample. One possibility of biasing a patient sample in favor of the biological types of schizophrenia lies in the selection of process schizophrenics. Hinsie and Shatsky(9) define process schizophrenia as a psychiatric state "connected with an organic process" and then make reference to Bleuler's statement that process schizophrenia is in that class in which "there is a morbid process in the brain that conditions the psychosis."

The definition of process schizophrenia may also be derived from Kraepelin's original designation of a dementia praecox(10). Nevertheless although this concept is as old as the concept of dementia praecox or schizophrenia, the problem of clarification remains. (We are *not* now considering the so-called schizophrenic reaction which is related to a known organic abnormality, for example a schizophrenic reaction resulting from an epileptic focus.)

Although "process" is often equated with the "organic," there seem to be myriad ways of arriving at this equation which may be relevant to the proposition of bias.

One way would be the "organic by analogy" school. The following summary is from an article entitled "Schizophrenia and Central Nervous System Pathology" by Brackbill and Fine(11).

> This study attempted to investigate some of the dimensions of schizophrenia. Three groups of subjects were studied: a group diagnosed as typical process schizophrenia, an atypical or reactive group of schizophrenics, and one with known central nervous system pathology. Rorschach protocols were examined for the incidence of Piotrowski's ten signs of organic involvement. It was found that the organic and process groups could not be distinguished from each other, but both of these groups showed significantly more subjects with at least five signs than did the reactive group. It was suggested that the difficulty in differential diagnosis of some kinds of schizophrenics and organics results from the involvement of central nervous system pathology in process schizophrenia. It is suggested that research findings would be less equivocal in studies of schizophrenics if this possibility were considered in the selection of subjects for investigations of schizophrenia.

Setting aside the question of reliability of Rorschach diagnoses of organic involvement and of reasoning by analogy (that is, through the intervening variable of the psychological projective-technique test), we must still consider process schizophrenia in determining our selection bias.

Most frequently, process schizophrenia is viewed as a constellation of signs, symptoms and predictions. In such a constellation, the following items are usually considered: 1. The premorbid history and personality. 2. Signs and symptoms. 3. The "Non-Reactive" versus the "Reactive." 4. Implications of psychological tests. 5. Course and prognosis.

In general, the premorbid history is described as schizoid. This is derived from a pattern of behavior in childhood, adolescence and adulthood(12). The question of childhood schizophrenia may be raised. Exacerbation of maladjustment may occur in adolescence. A bizarre differentness is usually in evidence. Premorbid performances in schoolwork, family relationships, social and sexual adaptation are said to prognosticate the malignant course and outcome(13). The increasing massiveness of symptoms is often noted. Symptoms usually emphasized include: depersonalization, derealization, pervasive ideas of influence, stereotypy, automatism, negativism, realization of disintegration of personality, *etc.* The onset is slow, insidious and from all available evidence not related to an acute or extreme stress (non-reactive versus reactive). Rorschach signs of organic involvement are present as are findings indicative of thought disorders. The course is regarded as progressive and deteriorating. Thus, regardless of the qualitative or quantitative aspects of symptoms, early improvement would render the diagnosis of process less tenable. In the general differentiation of process, asthenic and pyknic body types are said to be associated with the poor prognosis. Although there has been no systematic attempt to include a variety of biological test responses in differentiating process, many may be relevant.

It is important to emphasize that each of these items singly or in combination has been variously used as necessary or sufficient for the diagnosis of process schizo-

phrenia. Usually all of these concepts are blended under the definition of process schizophrenia. In our opinion, neither the equation, "process equals organic," nor the very definition of process has been sufficiently clarified for use in patient selection. Nevertheless one or more of the items noted may be used to examine subgroups and/or individuals within our sample. Thus, there should be the opportunity to compare process designations with genetic designations as well as with biochemical measurements.

Catatonic and hebephrenic subtypes as the basis of a biased sample. In such an approach, the assumption is made that one classical subtype is more likely to be biological than another. The evidence may include genetic and biochemical data. For example, Kallmann(14) found that the expectancy of schizophrenia is about twice as high for the children of patients in hebephrenic and catatonic groups (20.7% and 21.6%, respectively) as for those in the simple and paranoid groups (10.4% and 11.6%, respectively). Also according to Kallmann's data, there is a higher incidence of parental schizophrenia among hebephrenic and catatonic patients than among simple or paranoid patients.

Periodic catatonia is thought to epitomize this concept and many investigators consider this type a separate entity. Biological findings which relate to or precede recurrent episodes of illness have been reported(15).

A genetic approach as the basis of a biased sample. Planansky(16) summarizes the results of genetic studies of schizophrenia as follows :

> The reported excess (as compared to incidence of schizophrenia in the general population) of the studied psychoses in close relatives of psychotic probands is an indication of a certain degree of genetic predisposition even if the expectancy rates are the result of several modes of heredity and even if some proportion of the cases is independent of any specific genetic determination.

Our strategy then moves one step further. We have noted our assumptions relating to the (inconstant) biological types of schizophrenia. At this point, we seek to define these types in terms of a genetic inheritance. As indicated in the discussion of biological versus environmental factors, if genetic factors are unimportant, then our selection method may be irrelevant.

What approaches then have provided evidence for a genetic etiology of schizophrenia ? And can any of these be utilized to bias our sample ?

Twins concordant or discordant as to schizophrenia may be of use. In a number of reports, Luxenburger, 1938(17), Rosanoff, 1934(18), Kallmann, 1953(18), Slater, 1953(19), a comparative investigation of concordance in hospital patients reveals that there is a significantly greater concordance in monozygotic pairs. The absolute values of concordance rates advanced by different investigators are of less importance than the marked difference in concordance between the two twin categories.

Are twins useful in obtaining a genetically biased sample ? Allen(20) points out that "the relationship between identical twins is unique and despite the coefficient of relationship of 1, disease found in both members of a one-egg pair cannot so safely be attributed to a major hereditary defect as disease found in two ordinary siblings."[5] Monozygotic twins, in addition to having identical genes, also have identical constellations of genes. Since this is so, any phenotypic, biochemical alteration found in such twins might be due not to discrete genetically determined characteristics but, instead, to a characteristic determined by the entire constellation of genes. Such a constellation might not be duplicated by other sets of twins nor by other non-twin schizophrenics. (Tests performed on concordantly schizophrenic identical twins may be nearly equivalent to doing the same test twice on the same individual and, therefore, to halving one's sample. Of course, one member of each monozygotic pair may be used instead.)

Similarity of environment for monozygotic twins has been used to question the emphasis placed on twin studies. One an-

[5] If instead of a major hereditary defect, a complex genetic etiology were a central hypothesis for our selection, then monozygotic twins concordant as to schizophrenia, could constitute the desired biased sample.

swer to such questioning is the magntitude of the difference of concordance rates between mono- and dizygotic twins. The comparison of identical twins discordant for schizophrenia or else concordant but separated at birth, would permit useful and differential perspectives.

The existence of a schizophrenic gene or constellation of genes has been suggested but not established by analyses of sibships and other family groupings. Geneticists, analysing pooled data on schizophrenia, have been primarily interested in the underlying mode of inheritance, that is, whether of dominant, recessive or an intermediate form. In addition, the concepts of multiple additive factors and low penetrance have been utilized. Further, body build as a modifying influence controlling not only the penetrance of the gene but also phenotypic variation and the degree of malignancy, has been postulated. Several types of inheritance may play a role in the determination of schizophrenic psychoses.

Although twin studies are more widely known, family studies in schizophrenia preceded such studies and are more numerous. Indeed genetic theories originated in the observation of an increased incidence of schizophrenia in close relatives of schizophrenics. Biasing the selection in favor of patients with increased familial incidence seems reasonable.

If schizophrenia is etiologically diverse and includes cases with a simple genetic cause, these are the ones most likely to have underlying gross chemical pathology. In this manner we have thought of biologic in terms of inheritance, and have sought to link inheritance to the biochemical.

In planning the selection of schizophrenic patients for intensive biochemical investigations, it was decided that the widest sampling of genetic cases of the type desired would be achieved if one-fourth of the sample showed a family history suggesting dominance; one-fourth, a history suggesting recessiveness, and one-half, a negative family history. The rationale was that any common genetic type would be likely to occur among the patients with affected close relatives, but that any possible two-factor or semi-lethal dominant type might be crowded out of the family history groups if a significant percentage of cases of schizophrenia is truly due to a common dominant defect, to polygenes, or to environmental causes. The patients with negative family history would then be more likely to include the uncommon genetic types; even common genetic types of schizophrenia are apt to enter the negative family history group if genetic types have a high incidence. Such patients could, by design, also include any distinct clinical types not found in the first half of the sample(21).

In a small sample, it is possible for our selective criteria to exclude the very group for which selection-bias is intended. Selecting one-half of the sample without (immediate) family history of schizophrenia renders this exclusion less likely. An additional argument for such a procedure is in the consideration of patients in the family history group as particularly disposed by their environment to schizophrenia; if this is so, the patients in the negative family history group may reflect the stronger genetic disposition.[6]

THE APPLICATION OF A GENETIC DESIGN IN CURRENT INVESTIGATIONS AT THE NATIONAL INSTITUTE OF MENTAL HEALTH

The genetic design is based on the presence of schizophrenia *within* the immedi-

[6] On the other hand, we may also consider the patients in the Negative Family History Group as particularly disposed to schizophrenia by their environmental-learning situation and/or symbiotic, "pseudosupportive," ambivalent or "communicatively incongruent" relationship to a non-psychotic or non-overtly psychotic parent or significant "other." If this is so, the patients in the Family History Group may reflect the stronger genetic disposition. (Although we have indicated our operational assumptions we may conceptualize a series of genetic *and/or* psychogenic continua which may be useful in the study of family units containing a schizophrenic member.) As in the case of twins, individuals or siblings born into one family pattern, genetically or psychogenically defined, but reared from birth in a contrasting pattern or else a family without a schizophrenic member would permit useful and differential perspectives.

Within the group of patients or families selected by this primary mode of biased selection, random sampling may occur or else further purposive selection based on representation or distribution of sociocultural and psychological (personality) variables may be considered. In any case, such additional factors can be evaluated.

ate family of the patient. Even if simple Mendelian inheritance is unlikely, some family patterns of schizophrenia may be considered as more likely to be related to genetic factors than others. Affected relatives may constitute evidence for either recessive or dominant inheritance. Thus, there will not be a necessary correspondence between mode of inheritance and family patterns by means of which the cases are classified.

1. *Family History Group: The Dominant Pattern.* Typically a dominant pattern would require the presence of schizophrenia in one parent, 50% of the proband's children and 50% of the proband's siblings. Our *minimal* condition is one affected parent.

2. *Family History Group: The Recessive Pattern.* Typically, a recessive pattern would be fulfilled where neither parent is schizophrenic while 25% of the proband's siblings and a smaller percentage of his children are diagnosed schizophrenic. Our *minimal* condition is neither parent affected but with at least one affected sibling.

Examples will be given shortly of these two patterns.

Additional factors given positive weight in the selection of patients for either group include the presence of a normal sibling, the closeness, genealogically, of schizophrenic relatives and the frequency of schizophrenia in the entire family.[7]

Environs for two siblings, although diverse in many aspects will still share certain forces in common; the fact that such environs can also produce a normal sibling will be relevant. Appearance of disease in different (maternal, paternal) but related family units provides further evidence of etiology independent of the immediate family setting.

3. *Negative Family History Group.* Here the minimal requirement is availability of parents and siblings to rule out presence of schizophrenia within the family unit.

As previously noted, there may be more evidence for genetic inheritance in one subtype of schizophrenia as compared to another. Recognition of the possibility of differences in genetic disposition between subtypes may be used to modify our selection procedure. (The different clinical pictures may reflect a variety of additional circumstances which are required for the expression of genetic factors.) Thus if certain types of schizophrenics are excluded by the familial criteria, restoration should be made of representative subtypes (*e.g.*, simple, hebephrenic) in the Negative Family History Group.

Two examples of the Family History Group, Dominant Pattern, are seen in Figures 1 and 2.

Case 1: The patient (F. A.) is a 30-year-old, single, white male hospitalized since April, 1948. Diagnosis: chronic schizophrenic reaction, undifferentiated type with hebephrenic features. There has been no response to a variety of therapies.

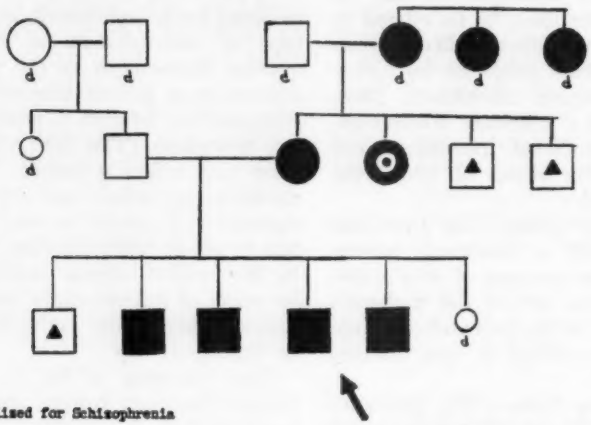
The patient's family history is characterized by the fact that his mother, maternal grandmother, 2 maternal grand-aunts and 3 siblings have been hospitalized for schizophrenia. A maternal aunt has been hospitalized for mental illness, type unknown. Two maternal uncles are alcoholic. The oldest brother may be alcoholic. The mother was a patient at the time of his admission. She had been hospitalized on several occasions during his early life and has been continuously hospitalized since the patient was 13 years of age. He is the fourth of 6 siblings. A sister died in infancy of a "bowel disorder."

Case 2: The patient (Q. M.) is a 29-year-old, white, single male who has been hospitalized almost continuously since November, 1950. Diagnosis: schizophrenic reaction, paranoid type with catatonic features. Hallucinations are prominent. There has been little apparent alteration of course with therapy.

Family history reveals that his mother, father, brother and sister have all been diagnosed as schizophrenic during the course of outpatient evaluation and therapy. A maternal uncle described as eccentric has also received psychiatric treatment. Only the patient and the maternal grandmother have been hospitalized for schizophrenia.

[7] The operationally defined dominant and recessive family patterns, these additional factors and many others will be relevant to criteria for the selection for longitudinal studies based on the expectancy of the appearance of schizophrenia within such families. The sample should also include negative history families and families without a schizophrenic member, for comparison. Thus both psychogenic and genetic hypotheses may be studied.

Figure 1. FAMILY HISTORY GROUP - DOMINANT PATTERN (PA)[1]



Hospitalized for Schizophrenia

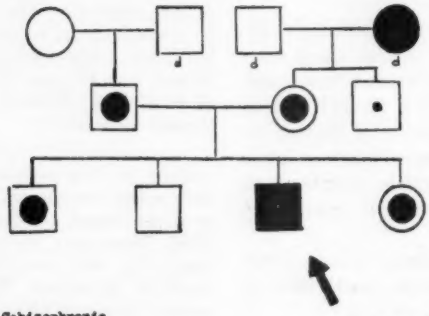
Hospitalized for mental illness, type unknown

Alcoholism

d died

1. Index Case is a 30 year old Undifferentiated Chronic Schizophrenic with Hebephrenic features, hospitalized, 1948

Figure 2. FAMILY HISTORY GROUP - DOMINANT PATTERN (Q.M.)[1]



Hospitalized for Schizophrenia

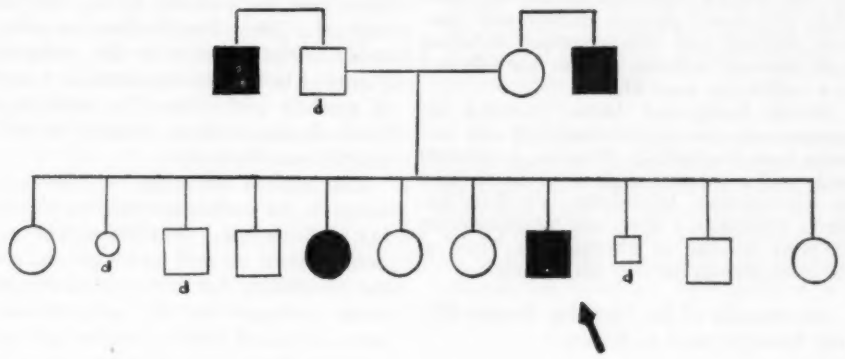
Non-hospitalized; diagnosis of Schizophrenia by psychiatrist

Mental illness, type unknown; psychiatric treatment

d died

1 Index Case is a 29 year old Paranoid Schizophrenic with Catatonic features, hospitalized, 1950

Figure 3. FAMILY HISTORY GROUP - RECESSIVE PATTERN (I.L.L.)[1]

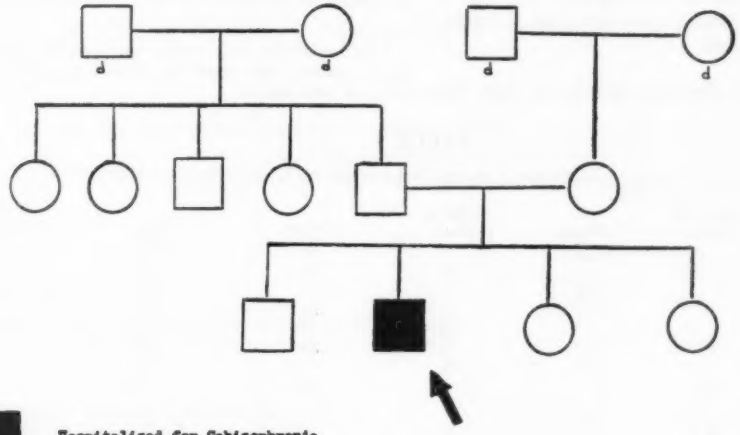


Hospitalized for Schizophrenia

d died

1 Index Case is a 36 year old Chronic Paranoid Schizophrenic, hospitalized, 1948

Figure 4. NEGATIVE FAMILY HISTORY (CA)[1]



Hospitalized for Schizophrenia

d died

1 Index Case is a 33 year old Chronic Paranoid Schizophrenic, hospitalized, 1953

An example of the Family History Group, Recessive Pattern, is seen in Figure 3.

Case 3 : The patient (I. L. L.) is a 36-year-old, divorced, white male with 3 children. He has been hospitalized almost continuously since 1948. Diagnosis : chronic schizophrenic reaction, paranoid type. His symptoms, including hallucinations, continue but he has adjusted to a withdrawn ward life.

Family background history revealed his parents were not psychiatrically ill and had never been hospitalized. However, a maternal uncle and a paternal uncle were hospitalized for schizophrenia. In addition, one of the patient's 10 siblings, a sister, was hospitalized for 11 years because of schizophrenia. None of the other siblings has ever been psychotic.

An example of the Negative Family History Group is seen in Figure 4.

Case 4 : C. A. is a 33-year-old, white, male, single, college graduate who has been hospitalized since July, 1953. Diagnosis : chronic schizophrenic reaction, paranoid type.

This patient's family history is, to the best of our knowledge, completely negative for schizophrenia. The family is characterized by high achievement. The patient's paternal grandfather and father are both educators. The patient's father is the oldest of 5 successful siblings. The maternal grandfather was a successful businessman. The patient is the second of 4 children. The oldest brother is an engineer and married. The patient's older sister is married to an engineer and has 2 children. The patient's younger sister, a teacher, is also married.

A scale for familial incidence may be utilized in the selection and evaluation of schizophrenic patients. The scale found in Table 1 provides a numerical score based on the sum of the coefficients (or closeness) of relationship of affected individuals to the index case, each sibship being represented only once(20).[8] Family data are also recorded in the notation of the pedigrees in Figures 1 to 4. Each key contains a number of symbols which may be used in each family-figure position ; symbol as well as position may be coded.

One implicit but major hypothesis in the rationale for coding evaluations of a number of factors, *e.g.*, familial incidence, genetic pattern as well as diagnoses, *etc.*, is the possibility that biological findings are often averaged out by comparisons between series of schizophrenics and normal controls. Even when there are one or more deviant findings, the usual approach is to repeat the experiment with another sample. However if subtypes exist, on whatever basis, it is possible that the next sample may not include a similar representative. If the finding is a borderline one, or perhaps emerges as a "cluster" within a normal range of values, the means for repeating and substantiating such data become even less likely.

Thus, by the use of criteria for selection as well as in the coding of identifying data, it should be possible to provide similar sub-

[8] This particular scale emphasizes dominant inheritance ; another scale might be devised to emphasize recessive inheritance.

TABLE 1

SCALE FOR FAMILIAL INCIDENCE IN THE SELECTION OF SCHIZOPHRENIC PATIENTS[1]

Parent	*Aunt or Uncle*	*Parent*	*Aunt or Uncle*	*Sibling*	*Score*	*NIMH Sample*
X		X		X	1.50	1
X			X	X	1.25	0
X		X			1.00	0
X				X	1.00	2
	X		X	X	1.00	1
X			X		.75	2
	X			X	.75	1
X					.5	0
	X		X		.5	0
				X	.5	1
					0.0	6

[1] Data refer to first 14 admissions

jects from previously screened reserves. This, of course, can be progressively differentiated. In addition, it would be possible to intensify a distinguishing characteristic, *e.g.*, a similar individual from a family history of recessive pattern, but with further indications of recessive inheritance. Obviously the biochemical differentiation of new subgroups would be in itself an important contribution.

Utilizing the criteria for selection as described, the patient population of 3 nearby hospitals was screened. Modification of the criteria for selection was necessary. Table 2 compares the selected Family History and Negative Family History Groups with the initial criteria for their selection. Table 3 reveals the decreasing number of subjects available as additional criteria for selection are imposed, *i.e.*, male, white, schizophrenic, age range, duration of hospitalization and familial pattern.

Data on schizophrenic patients from Family History and Negative Family History Groups, accepted for admission to the National Institute of Mental Health, are presented in Table 4.

The biological bias was kept primary and environmental factors were not considered in selection. Clinical status variables are also secondary in selection, but are likewise evaluated. Such additional data may in turn provide even more discriminating criteria for selecting new subgroups for biological studies.

TABLE 2

COMPARISON OF FAMILY HISTORY AND NEGATIVE FAMILY HISTORY GROUPS WITH INITIAL CRITERIA FOR SELECTION

	Initial Criteria	*Family History Group*	*Negative Family History Group*
Diagnosis	Schizophrenic	Schizophrenic	Schizophrenic
Sex	Male	Male	Male
Race	White	White	White
Age Range	20-35	29-41	25-37
Years Hospitalized	3-5	1-18	3-14
Availability of Parents	Alive and available	*	Alive and available

* Hospital records available for all family members diagnosed schizophrenic.

TABLE 3

SELECTION OF SCHIZOPHRENIC PATIENTS FOR BIOLOGICAL STUDIES : FAMILY HISTORY AND NEGATIVE FAMILY HISTORY GROUPS

	Referring Hospitals			
	I	II	III	*Total*
Number of Patients	2,800	3,500	7,200	13,500
Male	1,270	1,600	3,660	6,630
Schizophrenic	620	760	2,100	3,480
Age Range, 15-45 years	290	310	867	1,477
Age Range, 18-40 years, white, male Schizophrenic ; hospitalized more than 1 and less than 15 years	138	105	168	411
Family History*	24	15	20	59
Admitted	5	2	1	8
Negative Family History *	105	89	137	331
Admitted	2	2	2	6

* Only those members who clearly met the criteria for Family and Negative Family History designations are included. Histories for 21 families were insufficient for diagnostic purposes. Totals may be somewhat modified on the basis of on-going evaluations.

TABLE 4

ADMISSION DATA ON SELECTED SCHIZOPHRENIC PATIENTS[1]

	Age (Years)	Diagnoses *	Diagnoses **		Admission Data: First	Admission Data: Last	Admission Data: No.	Total Years
Family History Group—Dominant Pattern								
FA	30	Undiff.	Undiff.	(Hebephrenic)	1948	....	1	10
VG	35	Hebephrenic	Catatonic	(Hebephrenic)	1944	....	1	14
QM	29	Paranoid	Paranoid	(Catatonic)	1950	1951	2	8
GA	36	Simple	Undiff.		1940	1941	2	18
DQ	40	Hebephrenic	***		1937	1953	4	8
Family History Group—Recessive Pattern								
ILL	36	Catatonic	Paranoid		1948	....	1	10
EQ	41	Catatonic	Catatonic		1938	....	1	20
LQ	33	Simple	Simple		1947	....	1	11
No Family History Group								
CA	33	Paranoid	Paranoid		1953	....	1	5
KE	30	Paranoid	Paranoid		1954	1955	2	3
ILS	37	Catatonic	Undiff.		1942	1951	3	14
BL	25	Catatonic	Catatonic		1948	....	1	10
BI	27	Hebephrenic	***		1948	....	3	10
QB	33	Hebephrenic	***		1953	..	1	5

[1] White, male. Data refer to first 14 admissions.
* Discharge diagnoses at referring hospitals.
** Consensus diagnoses at National Institute of Mental Health. Parentheses indicate qualifying features.
*** Consensus diagnoses as yet not formulated.

Many questions relating to the biological and/or psychological may be raised by the composition of our Family History and Negative Family History Groups. (*The selection of schizophrenic patients for participation in family studies alone may be based on similar criteria.*) In what ways is the mother of one schizophrenic offspring different from the mother of 2 or more schizophrenic offspring? How do schizophrenics without a model for psychosis compare to schizophrenics in a family with 1, 2 or more models? How similar are such models? If there is schizophrenia in 3 generations and also related schizoid and healthy individuals in the family group, what information can be gleaned as to common psychological *or* biological findings? The selection of normal-control volunteers(2, 8) extends these research areas.

We may conclude that the process of selection of schizophrenic subjects for research study becomes an important part of the research itself.

SUMMARY

1. The method of selection of a small group of schizophrenic subjects for long-term biological studies is an essential part of the research. In developing criteria the following concepts are considered: (a) range of variation of irrelevant variables, (b) random sampling, nonpurposive bias and purposive bias, (c) extension of the sample and intensification of pertinent characteristics of patients through the process of selection and evaluation.

2. Variables presumbly irrelevant to schizophrenia are restricted: *e.g.*, age, sex, race, length of hospitalization and complications of hospitalization and treatment. The acceptance of limitations inherent in a chronic schizophrenic sample presupposes that schizophrenia is a reflection of an ongoing psychophysiological process (which however may appear only under certain operant conditions). The need for the study of acute schizophrenic and other samples is stressed.

3. An operational framework for biological versus psychological factors in schizophrenia is considered; the assumptions involved are tabulated. The working hypothesis assumes that there is a group of schizophrenias. Within this framework, process schizophrenics, catatonic and hebephrenic subtypes and twins concordant or discordant as to schizophrenia are discussed as means for sample bias.

4. A genetic-familial design is presented as the basis for a biased sample. It was decided that the widest sampling of genetic causes would be achieved if one-fourth of the sample had a family history suggesting dominance; one-fourth a history suggesting recessiveness, and one-half a negative family history. The patients with negative family history would be more likely to include an uncommon genetic type and also would render less likely the exclusion of the very group for which selection-bias is intended. The minimal conditions are as follows: (a) Family History Group—The Dominant Pattern; one schizophrenic parent; (b) Family History Group—The Recessive Pattern; neither parent affected but with at least one affected sibling; (c) Negative Family History Group; no history of schizophrenia within the family unit.

5. The decreasing number of subjects available from a patient population of 13,500 in 3 collaborating hospitals is noted as the following additional criteria are imposed: diagnosis of schizophrenia, male, white, age range 18-40, duration of hospitalization of more than one year and less than 15 years, and familial pattern. A comparison of Family History and Negative Family History Groups with the initial criteria for selection is made; data referring to the first 14 admissions are presented.

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THE PRACTICE OF PSYCHIATRY IN ENGLAND UNDER THE NATIONAL HEALTH SERVICE, 1948-1959 [1]

A. SPENCER PATERSON, M.D.[2]

It is a great privilege for me to be given this opportunity of reporting to you on the practice of psychiatry in England during 10 years of the National Health Service. I shall try to answer the questions, "How far has the psychiatric patient benefited, and what has been the impact of the Service on the psychiatrist's freedom of action and on his professional standing?"

In the last 25 years there has been an unparalleled advance in our knowledge of mental illness, especially in the sphere of therapeutics, and the world owes much to American medical science for originating or developing a number of fruitful procedures. Many British psychiatrists, like myself, owe a debt to American teachers which can never be adequately repaid. I was assistant in psychiatry at the Phipps' Clinic under Adolf Meyer and worked in Britain with the distinguished expounder of his doctrines, Sir David Henderson. I have also had the privilege of observing pioneer work at different centres in your vast country in the course of 3 previous visits.

When the visitor reflects on some of the greatest achievements of American medicine, he will no doubt realise that behind these achievements lies a tradition of individual freedom and enterprise, of healthy competition, and also of social service on the part of professional men and other citizens. At the same time the visitor may be led to doubt whether the medical profession together with the civic authorities and voluntary organisations have up till now created an efficient enough instrument to bring the benefits of all these medical and psychiatric advances to the average sick patient.

A study of recent American medical literature confirms the impression that there is an impending crisis with regard to medical administration. A statement for instance made by the Board of Trustees of the American Medical Association runs as follows:

> We can all agree that the American people should have access to the best possible health services. There is no debate on this specific objective. There is however divergence of opinion as to how and when this can best be accomplished (2).

This divergence of opinion apparently reflects the question whether private insurance will be the main instrument in providing the necessary services. Certainly at the present time medical insurance does not appear to provide an adequate answer to the problem of treating the psychiatric patient. A recent writer in the *American Journal of Psychiatry* states that only 10% of America's population is in a financial position to "buy" psychiatric care on the traditional "fee for services" basis.

> Thus 90 percent of our fellow citizens must look to the Government or private philanthropy to help them, or they borrow and build up a crushing burden of debt; or they just go without treatment. . . . In this country, current pressures for additional and more available psychiatric services can push us toward Government responsibility for all forms of psychiatric care.

The writer then says that there is another possibility which is more in line with social evolution in America. This would be a working partnership of voluntary and individual effort with help from the Government (1).

The degree to which many Americans are afraid of this Government help may be judged from the statement of a past Vice-President of the A.M.A. when discussing a dispute between the A.M.A. and the Veterans' Administration. He writes:

> The Veterans' Administration program is expanding government control over the nation's medical care system and is providing a big entering wedge for a complete Federal health program covering the entire population.

[1] Read at the 115th annual meeting of The American Psychiatric Association, Philadelphia, Pa., Apr. 27-May 1, 1959.

[2] West London Hosp., London, Eng.

The writer went on to state that the American Legion and the A.M.A. should be working together in the fight against Communism and also to defend the free enterprise system and to build up a positive understanding of Americanism(11).

We in England can sympathise with our American colleagues when they are apprehensive with regard to the ultimate consequences of submitting the medical profession to some degree of Government control. We had some of these same fears in 1948, but I am bound to say that after 10 years of the National Health Service, most psychiatrists would agree that the benefits which have accrued to the average citizen who is suffering from neurotic or psychotic illness, and also certain improvements in the conditions of work for the psychiatrist have up to the present at least outweighed any disadvantages of the system.

The distinguished writer whom I have just quoted mentions Communism but there are of course many essential differences between the National Health Service in England and the system of state medicine in Russia. I cannot speak with authority on the Russian system, as I have not visited that country since 1929, but some of its characteristics have been described in the following terms. Medicine has been entirely subjected to the goals of the regime. The Government could not therefore tolerate any independent professional body of doctors. The medical man does not apparently think of himself so much as practising a profession as being a member of a Trade Union. According to Russian ideology the aim of the medical profession is to prevent and to treat illness because it hinders productivity. The Russian physician is thought by foreign critics to be imbedded in a bureaucratic structure which is controlled by a political party. His first duty is thought to be not to the patient but to the State.

Under such a system various evils are said to ensue. Unsuitable orders reach the periphery from the central authority and these must be either disobeyed or else "formally" obeyed but disobeyed in spirit. This is obviously bad for the morale of the physician, while the administrators working at a distance get out of touch with what is happening at the doctor-patient level. It is said that initiative and enterprise at the periphery are stifled by too many directives from the central authority. Further, conscientious practitioners may be intimidated by threatening letters in the Press or by branches of Trade Unions. The authorities may favour the appointment of a doctor to a responsible post by reason of his politics rather than for his technical skill.

These are some of the criticisms directed against the Russian system by refugees who eventually reached America from the Soviet Union. Nevertheless these same refugees stated that this system of medical care had hitherto been unsurpassed in their country and even those refugees who had personally had unfortunate experiences under the system emphasised that in their opinion some form of state medicine was preferable to one based on free enterprise (5).

Medical men in Russia after the Revolution were faced with a different problem from that which existed in England in 1948. Their task was to create a health service as quickly as possible for their gigantic population where almost no service already existed, and so they went about the problem, not unreasonably, as if they were planning a huge military campaign. The enemy in this case however was not a hostile state but disease in its various forms. But when the National Health Service was introduced into England in 1948, the situation was quite different. The new British service did not entail a complete break with the past. On the contrary the aim was to absorb all that was good in the existing services into the new scheme. Parliament intended that the benefits which had been available only to insured persons, or to those who could afford them, or receive them as a form of charity, should now be available to everyone. At the same time the essential freedoms were to be safeguarded. The citizen was free to use the Service or any independent part of it, as he pleased. He was free to choose his own doctor and to change to another if he so desired. The doctor on his part was free from interference in his clinical judgment and was free to make any criticisms of the Service which he wished. He could accept

private patients while taking part in the Service, or again, he could have an entirely private practice and so remain outside the Service.

It should be noted that the creation of the National Health Service did not constitute a Party issue but was supported by all Parties, including the Conservatives. The Service is now being used by 97% of the population. The great majority of specialists, 90% of family doctors, and almost all druggists, are co-operating in the scheme.

It is of interest that when the scheme was initiated the late Lord Horder founded the Fellowship for Freedom in Medicine. This body has regularly published a journal which keeps a close watch on the medical man's professional freedom and interests. It has recently advocated a system of State Insurance through which it is hoped to save more of the Exchequer's money while giving more responsibility to the family doctor. There is however almost no chance that this scheme will be supported by any political party. The present system is too popular with the public for that. There is however an increasing number of citizens who are taking out private health insurance policies, but this is no reflection on the efficiency of the National Health Service because most patients who do this are merely aiming at securing better amenities during treatment. A proportion of them however pay sufficiently high premiums to enable them to have treatment wholely outside the Service. This development will therefore entail more private practice for the part-time psychiatrist in the future.

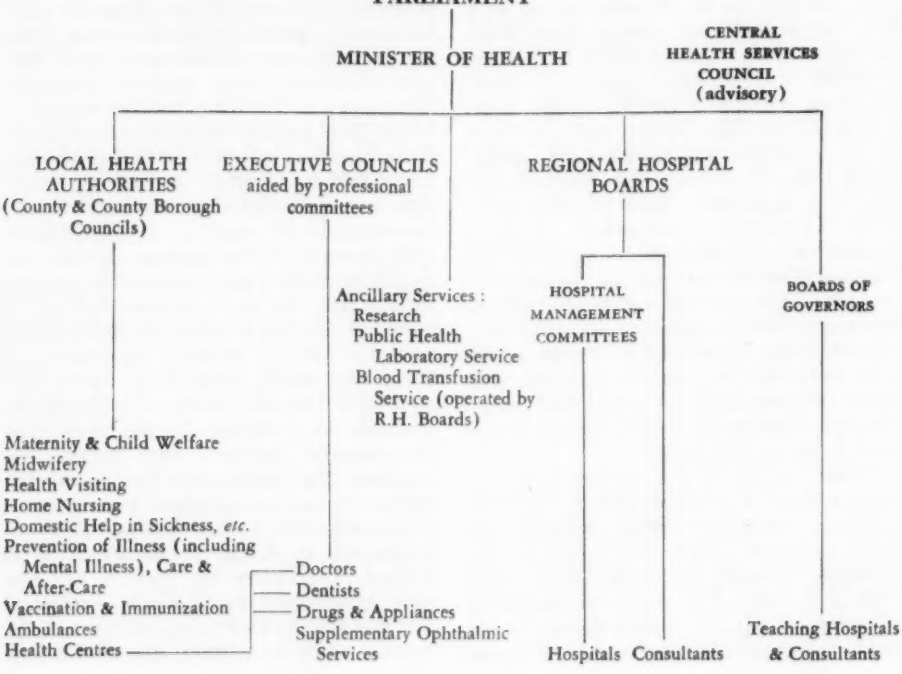
THE MACHINERY OF THE NATIONAL HEALTH SERVICE

The Service in Britain is administered centrally by the Ministry of Health advised by a Central Health Services Council and various committees. There are 3 main divisions of the Service(6).

1. Hospital and Specialist Services.
2. Local Authority Services. After-care,

TABLE 1

ORGANIZATION OF THE NATIONAL HEALTH SERVICE IN ENGLAND AND WALES



maternity and child welfare, midwifery, health visiting, domestic help in sickness, prevention (*e.g.* vaccination), ambulances and health centres.

3. Practitioner and Dental Services.

With regard to the first division, the 14 Regional Hospital Boards, which look after regions with populations varying from 1 to 3 million, are responsible for all the mental hospitals (147,000 patients) and all the mental deficiency hospitals (60,000 patients) and for the outpatient services (3, 8).

Secondly, the Local Health Authorities are responsible for the care of the defectives in the community (80,000) and for the prevention of mental illness and for the after care of those who have been in mental and mental deficiency hospitals. The Medical Officers of Health are now tackling the problems of mental health which impinge on their sphere of activity with the same enthusiasm with which they had previously overcome the threats of infectious diseases such as cholera, enteric fever, diphtheria, and the like. Their Society has recently established a mental health group and there is now more psychiatry in the syllabus of the course for the Diploma of Public Health. There is therefore good reason to hope that with these new-found allies, we psychiatrists will make still further progress in the coming years in our struggle against mental ill health.

Thirdly, the family doctors are much more interested in psychiatry than formerly. The newly founded College of General Practitioners has published a Report (4) which discusses such questions as how to improve the quality and quantity of psychiatric education both for the undergraduate and for the postgraduate practitioner. The family doctor in the future may be expected to look after the mental health of his patients with more understanding than previously when he relied mostly on intuition.

BENEFITS ACCRUING TO THE PSYCHIATRIC PATIENT FROM THE NATIONAL HEALTH SERVICE

The first indication in the campaign against mental ill-health was to treat as many patients as possible and at as early a stage in their illness as possible. Accordingly some 500 new outpatient departments have been started in the past 2 or 3 decades and many of these in the past 10 years. They are mostly attached to general hospitals(9). Where the hospital is a teaching one, there is generally a number of beds which are used for research and teaching. It is reckoned that the psychiatric patient is willing to go to such a clinic 12 or 18 months earlier than he would be willing to go to a mental hospital. There has been at the West London Hospital an increase in the number of patient-sessions per annum since 1945 to the extent of about 500%. The number of psychiatrists has gone up from 3 to 10 and the non-medical staff has been correspondingly increased.

There has also been continuous research, mostly into active methods of therapy, particularly electrocerebral treatment, ataractic drugs, and hypnosis. These are subjects suitable for research in a general hospital where collaboration with colleagues in other disciplines is possible. This does not mean that psychotherapy is neglected. However, as in America, much thought is given to the possibility of shortening the duration of treatment while achieving an equally good result.

Our clinic is merely one of many, but when such clinics are multiplied to the extent of some hundreds, then results begin to show in statistics.

Not only has the number of clinics increased, but under the National Health Service the number of consultants has increased to a greater extent than in any other specialty. In 1949 there were 405 but in 1957, 614, an increase of 52% compared with an average 32% increase in other specialties. Similarly the trainee-specialists (senior registrars) have risen from 113 to 144, a greater increase again than in other branches of medicine. This should be of interest to American psychiatrists, for recent publications have deplored the lack of trained psychiatrists in mental hospitals(10).

The training of the psychiatrist is much more thorough nowadays than it was before 1948. He is encouraged to take a higher diploma in internal medicine as well as one in psychiatry. He is expected to be as equally at home in giving different

forms of physical treatment as he is with psychotherapy. Young psychiatrists, especially those residing near London, often undergo at their own expense a long and expensive training analysis with a view to future practice of this method.

With regard to inpatient treatment in mental hospitals, this can be conveniently divided into short stay and long stay. Since 1946 the number of patients admitted to mental hospitals has much more than doubled, from 36,000 to 84,000, an increase of 125%. The percentage of patients discharged within 3 months has risen from 50 to 55% in 2 years, and from 65 to 69% for those discharged within 6 months. This more than doubling of the numbers of short stay patients has of course greatly increased the amount of work done by mental hospital psychiatrists, but the actual number of beds occupied has actually fallen within that period by 1,353(9).

Recently however, there has been an even more striking trend. The question was asked, why should not a large proportion of these short stay patients be treated outside a mental hospital? Dr. Carse in 1956 organised "The Worthing Experiment" in which psychiatrists visited patients in their homes and, where necessary, gave them energetic treatment in an outpatient clinic or day hospital. It was found in this way that in a rural area a reduction in the rate of admissions by 57% could be achieved. A surprising feature of this study was that a high proportion of the patients who recovered without going into hospital belonged to the class over the age of 65, where one would have supposed that the prognosis was particularly poor.

With regard to the long stay patient equally striking experiments are being carried out(7). As in America, the greatest efforts are being made to rehabilitate long stay patients who have shown some response to treatment with electroshock and ataractic drugs(12). The services of experts in sociology and group psychology have been enlisted, as at Netherne under Freudenburg(8). Elaborate measures are taken to train the nursing staff and secure their co-operation in what is a particularly arduous task. The patients are gradually subjected to work therapy, and at Banstead a factory actually exists inside the hospital. These measures are carried out in a particularly humanitarian atmosphere. There is a growing tendency to do away with locked doors. Attempts are made to invest the recovering patient with a new dignity. He is now called "Mr. Smith" instead of just "Joe." There is an increase in the mingling of male and female patients with a notable improvement in their manners and behaviour.

Before this new development the percentage of patients who had been in a mental hospital over 2 years and who became well enough to leave the hospital was only 2% per annum. It is likely however that in the future this figure will be increased to 10 or 20%.

It is because of the rise in numbers of successfully treated short stay patients and to a lesser degree of long stay patients that the Royal Commission on Mental Disorder and Mental Deficiency, 1956, was able to recommend new measures which are incorporated in a Bill now before Parliament (8). One result of this will be to arrange for the more effective care of recovered mental patients and improved mentally defective patients in the community. New measures will include the establishment of hostels, day hospitals, homes for the aged and the like. The new Mental Health Bill also aims at a more rational approach to the problem of mental disease, bringing it more into line with the rest of medicine.

I realise of course that the great advances in treatment to which I have alluded, have been equalled, or even surpassed, in some other parts of the world, especially America, but the point I wish to make is that in our country the improvements in therapy have been brought to the ordinary citizen to a far greater extent than would have been possible if it had not been for the National Health Service. It is certainly true that any fears which might have been entertained that socialised medicine might stifle initiative among practitioners working at the periphery have not been realised. On the contrary, there has been a new enthusiasm which has in large measure been responsible for these new developments.

It may perhaps be added that the smooth running of the Service has been helped by particularly good relations which have ex-

isted between psychiatrists and the public, the latter including members of the Civil Service. This goodwill has been greatly fostered by a series of programs on radio and television, and in the press. It is to be hoped that such publicity will continue, because only in this way will the citizen appreciate what he is receiving in return for the taxes which he pays to support the Service.

PRIVATE PRACTICE UNDER THE NATIONAL HEALTH SERVICE

Only 2% of approved mental patients are treated privately(9) but in spite of this there is still a considerable amount of private practice in psychiatry, mostly in urban areas.

In the years before the war the prospects of a career in psychiatry were not very attractive. An article in the *British Medical Journal* in 1937 stated that nearly all psychiatrists were whole-time officers in mental hospitals and that the pay was poor and the chances of promotion were limited. A brighter prospect however was presented to the relatively small number of psychiatrists who could procure a post in a general teaching hospital where they could combine the teaching of students with opportunities for research and also carry on a consultant practice. Such a life however would be a hard one with little time for leisure and their hospital work would not be remunerated.

In London and some other cities there were also doctors specialising in psychotherapy and there was the Institute of Psychoanalysis. One-third of the psychoanalysts had no medical degrees. Many so-called psychotherapists had no senior qualification.

The following were some of the changes which occurred in the mode of life of the consultant at a teaching hospital, when the National Health Service was initiated in 1948. We were no longer honorary psychiatrists at our hospitals but received salaries for our attendances there. We were free to decide whether we would work for any number of half days up to 9 in the week, 11 half days being counted as a full week. Most of those working 7 or 9 half days are employed at more than one clinic. We were of course free to remain outside the Service if we so desired.

For those working full time the salary scale is roughly as follows : A young consultant at the age of 30 has about £2,000 a year rising to a maximum salary of £3,-385 a year. There is however a system of merit awards by which 20% obtain an additional £500, another 10% an additional £1,500, and another 4% an additional £2,500 over the basic salary. Recently the sum of £300 has been subtracted from the highest merit award and £200 from the second highest, apparently indicating a new egalitarian trend.

The pension amounts to 1.5% per annum of all the money which has been earned under the Service. This compares favourably with other schemes of a like nature.

The Ministry encouraged psychiatrists to visit patients in their own homes. In this way the specialist can discuss the case with the family doctor and also observe the family setting. In many cases this has enabled active steps to be taken at the earliest possible stage of the illness. The psychiatrist is paid 4 guineas (about $12) for the visit, plus a travel allowance. He may earn some 800 guineas a year over and above his basic salary in this way.

The same applies to the full time man but in his case the first 28 visits in each quarter are unpaid except for the travel allowance.

Those who prefer whole time service have benefited under the Service because a number of new and attractive posts have been instituted. There have been 9 new whole time professorships at provincial universities, and some two dozen appointments of whole time research workers who initiate and organise research projects which are often common to different hospitals in the same group.

For those who are part time there is still a great deal of private practice in London. As already mentioned there is an increasing number of citizens who have taken out a health insurance policy. This will enable the patient to see the psychiatrist privately and to obtain better amenities under the Service. If the premium is high enough it will enable the patient to receive treatment in an expensive room under the National Health Service or else outside the Service altogether.

There is another source of private practice. There are many visitors from overseas, especially in summer. These are not British subjects but are glad to avail themselves of recent progress in psychiatric treatment. They often provide a colourful change from our more humdrum work.

There still appears to be a considerable demand for private psychotherapy in London and possibly to a lesser extent in other cities. In addition to the part-time consultants already mentioned, there are a number of psychotherapists who do private practice but who also work at a clinic like the Institute of Psychoanalysis. There are also practitioners who are entirely in private practice. Many of these write books on popular psychiatry for the general public. Some of them, however, have not had any adequate training nor any diploma in psychiatry, and are sometimes referred to as "consultoids." Their success to some extent depends on the fact that the public as a whole looks on a Harley Street address as a kind of medical degree. By way of contrast to these practitioners there are a number of distinguished psychiatrists who have retired from the Health Service and who are now in full time practice. A few psychiatrists of repute work in private institutions and also engage in consultant practice as well.

Conclusion

In conclusion I should like to say that in America and Britain psychiatrists are striving towards the same goal, for we are trying to give the best possible psychiatric treatment to the greatest number of citizens who require it. In Britain however it was decided after the war to conduct the struggle against mental illness at the National level. I have therefore attempted to give you some account of how far our efforts have succeeded and of how far in doing so we have preserved our ancient tradition of professional freedom.

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PSYCHIATRIC DAY HOSPITALS [1]

MICHAEL CRAFT, M.D., M.R.C.P. Ed., D.P.M.[2]

A day hospital may be defined as one where full hospital treatment is given under medical supervision to patients who return to their homes each night. It offers an alternative to inpatient admission to those for whom outpatient treatment is inadequate. It is suitable for those of the mentally ill who are well enough to travel and to spend the night with their families.

REVIEW OF LITERATURE

In North America, Cameron(6) in 1947 described day hospital care in Montreal and first introduced the term to Western literature. He treated "early . . . or mild advanced types of schizophrenia. Both hypomanic and depressed patients have been successfully treated." There were both hallucinated patients and those with suicidal ideas. An important function of this unit was the care of convalescent inpatients. He stressed cheapness, swiftness of recovery and importance of easy transfer to bed wards. These have been recurrent themes in later publications.

The Menninger Clinic day hospital started in 1949, and Barnard *et al.*(3) reported that one-third of all patients were treated on a day basis. It provided foster homes for patients who lived out of town. The 109 patients stayed an average of 70 days each and 90 were convalescent inpatients. The patients included 33 schizophrenics and 33 with character disorder.

Moll(17) founded a day hospital in the Montreal General Hospital in 1950 on Cameron's pattern. He used all forms of treatment except coma insulin. Depressive illnesses occur first on his list of diagnoses, although no figures are given. He found acute psychotics and defectives unsuitable. Many of his patients were not sufficiently ill otherwise to need inpatient care.

Pottle(18) runs a day hospital in sparsely populated Newfoundland. Government subsidized transport and lodgings ensure attendance of patients at a specially designed day care unit in the first floor of a new mental hospital. All forms of treatment including coma insulin are given, one irreversible coma occurring in 5 years practice. Landladies are instructed in the treatment of hypoglycaemia.

Cameron, reviewing 9 years practice (7), decided that, as transfers from day hospitals to inpatient wards were "infrequent," the former could well be independent. However, patients with suicidal ideas and disturbing behaviour could best be treated first as inpatients. One suicide occurred in the period reviewed. He feels that coma insulin treatment is quite satisfactory on a day care basis.

Bierer(4, 5) described the first day hospital in England. It is entirely independent of mental hospitals. The frequency of attendance by patients varies from 1 to 12 or more times a week. It is designed to function as a community centre. All forms of physical treatment, apart from coma insulin, are used. He advocates group treatments and the advantages of independence are stressed.

Aron and Smith(1) describe the Bristol day hospital. Geographically apart, but run by Bristol mental hospital staff, transfer of patients to and from the mental hospital is simple. Forty-four percent of the patients had depressive illnesses. The average number of days attended was 21, attendance becoming less frequent as the patient recovered. Smith(19) reviewed 1,000 Bristol day hospital patients, of whom 16% had been convalescent in patients and 10.4% had needed transfer to bed wards. The proportion of depressions treated had risen to 57% in 1955 and 9% had schizophrenia. Coma insulin had not been used.

Cosin(8, 9) describes a geriatric day hospital. Since it is run as part of a geriatric hospital the 70 day patients required no extra medical staff.

Harris(13, 14, 15) has reviewed the de-

[1] I am indebted to Professor Aubrey Lewis for his encouragement and to Dr. Arthur Harris for his help and permission to use the clinical material of the Bethlem and Maudsley Day Hospitals.

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velopment of the Maudsley and Bethlem Royal Day Hospitals. Admission criteria are those appertaining to inpatient beds, and attendance 5 days a week is obligatory. Harris suggests that speedier treatment may be possible in day hospitals, owing to the patient remaining in his home surroundings.

In Nigeria, Lambo(16) has adapted the day hospital idea to an African community and uses a day centre with night foster homes. He uses both insulin coma treatment and ECT.

The first day hospital in Russia started in Moscow in 1932(11). Day hospitals were considered as departments of mental hospitals and where the latter were overburdened were intended to take on all their functions. The Moscow day hospital treated 1,225 patients in 4 years, 47% having schizophrenia, 30% neurological diseases including taboparesis, but only 6% with manic-depressive psychosis. Practice and results were further reviewed after 12 years (12).

DIAGNOSTIC CATEGORIES OF PATIENTS TREATED

This can be illustrated by figures drawn from published data, analysis of patients treated at the Maudsley Day Hospital over a 3 year period and personal communication from Bierer and the South West Regional Hospital Board.

Diagnostic usage almost certainly varies between countries, but it is clear that day hospitals can be adapted to deal with widely different groups of mentally ill patients. In England depressive illnesses account for a considerable proportion of those treated.

ENGLISH DAY HOSPITAL PRACTICE, 1956

Enquiry at the Ministry of Health revealed that at least 10 day hospitals were open in England in 1956. The author worked at the Bethlem Royal and Maudsley day hospitals. To investigate practice elsewhere, those units treating more than 10 patients daily were either visited (The Marlborough, Bristol and Oxford Day Hos-

	Dzhagarova 1937	Menninger Clinic Barnard 1952	Bristol (SWRHB) 1957	Marlborough Day 1956	Nigeria Lambo 1956	Maudsley Day 1953-56
Schizophrenia	47%	30%	10%	35%	24%	8%
Manic-depressive psychosis	6%	7%	29%	3%	6%	25%
Involutional melancholia		6%	11%			11%
Other psychoses	38%	2%	2%	—	16%	4%
Neurotic depressive reaction			33%	38%		28%
Anxiety neuroses		25%	9%			12%
Psychoneuroses and others	9%		8%	24%	54%	7%
Personality disorders		30%	4%			5%
Relevant numbers of patients	1225	109	342		146	300
(Total depressive illnesses)	6%	—	73%	41%	6%	64%

pitals) or discussed with their Directors (Oldham and Birmingham).

Two types were found. The Marlborough under Dr. Bierer was entirely independent. The other type was associated with a parent mental hospital: the Bristol Day Hospital under Dr. Smith, treated general psychiatric patients; at Birmingham, under Dr. Mayer Gross, there was an experimental unit treating chronic neurotic patients, many on National Assistance; the Oldham Day Hospital under Dr. Pool, was a unit in a community care programme; Oxford, under Dr. Cosin, treated mentally and physically ill geriatric patients; the Maudsley and Bethlem accepted only those who would otherwise have needed mental hospital admission.

The main group of patients admitted to day units were those for whom outpatient treatment was inadequate or unsatisfactory, but who did not require admission to the acute ward of a mental hospital. The day hospital contributed most to the reduction of inpatient waiting lists, when it accepted only patients who would otherwise have required inpatient admission, as at the Maudsley. It also functioned as an alternative to outpatient treatment when a number of part time attenders were accepted, as at the Marlborough. Most day units found it convenient to treat both those needing full time and part time treatment.

The psychoneuroses were most successfully treated at day hospital level. The majority of depressive illnesses would fall into this diagnostic group. Depressive illnesses were the major diagnostic entity for each of the English day hospitals from which figures were available. With psychoses the acutely disturbed were clearly unsuitable, but a considerable number of schizophrenic patients could be treated at day hospital level. The Maudsley accepted patients with a depressive psychosis, but none who presented immediate suicidal risks, and there were no suicides in a 3 year analysis. The acceptance of the seriously ill was found to depend upon the quality of home care available.

There was a wide measure of agreement on the methods of treatment used. A general emphasis on group activities was found, group discussions being a feature of most units. English day hospitals did not use insulin coma therapy, although this has been used elsewhere, admission being favoured on the grounds of safety. Electroconvulsive therapy was used in all units and the practice was to have patients escorted home afterwards.

The use of transfer to a parent hospital was carefully investigated as Cameron stated that the need for transfer was "infrequent." The available figures showed that the annual transfer rate of the Menninger Day Hospital was 16%, of the Bristol 10.4% and of the Maudsley 14.7%. The last two units definitely found transfer facilities valuable. Ease of transfer to a hospital bed at short notice contributes to the safe management of a day hospital, since sudden acute exacerbations of patients' illnesses are not uncommon.

The main factors limiting the use of day hospitals seemed to be the geographical situation and the quality of home care offered by relatives. A great expansion in this field, to cover much of the country, would seem both economical and feasible.

Summary

The literature on psychiatric day hospitals is reviewed and an account is given of day hospital practice in England in 1956, with respect to types of patients treated and treatment employed. It was found that day hospitals were treating a wide variety of mental illnesses, and that those treatments commonly employed in mental hospitals could also be used in day hospitals.

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CLINICAL NOTES

DEANOL (DEANER) IN THE TREATMENT OF SCHIZOPHRENIA

JOSEPH A. BARSA, M.D. AND JOHN C. SAUNDERS, M.D.[1]

Deanol (Deaner)[2] is the para-acetylaminobenzoate salt of 2-dimethylaminoethanol. It is the tertiary amine precursor of acetylcholine, and, unlike choline or acetylcholine itself, is able to pass freely across the blood-brain-barrier. The ability of deanol to increase cerebral acetylcholine has been postulated as the mechanism of its therapeutic action.

Deanol has been used chiefly as a central nervous system stimulant for mild depressions and chronic fatigue states. However, it has also been reported to be effective in chronic schizophrenics. This study was undertaken in an effort to confirm the latter results.

As a pilot study, 10 chronic schizophrenic females between the ages of 37 and 71, who had been continuously hospitalized for 5 to 27 years, were given deanol orally for 9 months in a single morning dose of 150-300 mgs. Within the first few weeks a mild stimulating effect was evident in 6 patients. They seemed a little brighter, more alert, more interested in their environment, although their delusions and hallucinations remained unaltered. However, in the subsequent months a further change slowly manifested itself in 2 patients. Their delusions and hallucinations seemed to be fading and were more difficult to elicit. It was concluded that deanol has 2 actions : a mild stimulating effect, and a moderate anti-psychotic effect (*i.e.* combats delusions and hallucinations of the schizophrenic). However, the anti-psychotic action was not as potent as that of the phenothiazines or reserpine. It was therefore decided to combine deanol with a tranquilizer containing a potent anti-psychotic effect.

Two hundred chronic female schizophrenics between 16 and 69 years of age were selected. They had been continuously hospitalized for 3 to 27 years, 145 having been hospitalized for 10 or more years. All of the patients had been receiving tranquilizing drugs for at least 18 months with slight or moderate improvement. However, for the last 6 months they had reached a plateau and no further improvement could be detected. It was at this point that deanol was added. One hundred twelve patients were receiving chlorpromazine, 5 proclorperazine, 70 a combination of chlorpromazine and proclorperazine, 6 reserpine, 4 a combination of chlorpromazine and reserpine, and 3 perphenazine. The dose of these tranquilizers was not changed when deanol was added. Deanol was given in a single morning dose of 25 to 100 mgs., the majority of patients receiving 50 mgs. Deanol in combination with the tranquilizers was continued for 6 to 13 months. At this time 84 patients were unchanged ; 99 were improved, 17 being markedly improved, *i.e.*, either released or ready for release from the hospital. Of the markedly improved patients 9 had been continuously hospitalized for 3 to 5 years, and 8 patients for 7 to 19 years.

It was again observed that the clinical effects of deanol manifested themselves very slowly. It usually took several weeks for the full stimulating effect to develop, and several months for the full anti-psychotic effect. Deanol did not produce euphoria ; patients became less withdrawn, more alert, interested and energetic. There were no serious side-effects. Ten patients receiving 100 mgs. complained of anorexia, and two complained of jitteriness, but these symptoms disappeared when the dose was lowered to 50 mgs. There was no interference with sleep, and no evidence of tolerance to the drug.

From this study, it can be concluded that deanol, when combined with a tranquilizer containing a potent anti-psychotic action

[1] Rockland State Hospital, Orangeburg, N. Y.

[2] Riker Laboratories Inc., Los Angeles, Calif.

is of definite value in the treatment of schizophrenia. Not only does its stimulating effect counteract the excessive sedation and lethargy produced by the tranquilizer, but its own anti-psychotic effect is additive to that of the tranquilizer.

A SAFE TRANQUILIZER: NIACINAMIDE HYDROBROMIDE AS A SAFETY FACTOR

HENRY M. FEINBLATT, M.D.[1]

Attempts have been made to define a tranquilizer as any sedative which accomplishes its sedation without causing a condition of areflexia. A safe tranquilizer which meets these requirements is afforded by a combination of ammonium and potassium bromides with niacinamide hydrobromide as a safety factor.[2] Its mild tranquilizing effect and freedom from untoward responses have made this medication the one of choice in ambulatory working individuals. The objection of bromide intoxication has been fully met by the introduction of niacinamide hydrobromide(1, 2).

Tranquilizers, both new and old, have their specific side-effects and toxic reactions. Any method of overcoming these undesirable reactions is a step forward(3). Thus, the step of utilizing niacinamide hydrobromide to overcome the side-effect of bromide medication is a definite contribution to therapy.

Bromism depends upon 3 factors: (a) bromide concentration in the blood, (b) genetic predisposition (idiosyncrasy), and (c) the co-enzyme factor(1).

The first two factors are obviously involved in any medication and the characteristic unique feature of bromism has been the poisoning effect exerted by bromides on the respiratory co-enzyme mechanism, the di- and tri-phosphopyridine nucleotides (co-enzyme I and II). Disturbance of this co-enzyme mechanism can make the person uniquely sensitive and even cause bromide intoxication at low blood concentration levels. When the essential portion of the nucleus of the co-enzymes is supplied in the form of a pyridine metabolite (niacinamide hydrobromide), bromism does not occur.

The clinical syndrome of pellagra is analogous to, and has many of the characteristics, signs, and symptoms of, bromism,—that is, the cutaneous, digestive, and nervous changes induced thereby. Pellagra is also controlled rapidly by the use of a specific source of the pyridine nucleus such as nicotinic acid (3-carboxypyridine). The acneform and other irritative lesions on the face and exposed part of the body of both pellagra and bromism are quickly cleared when this essential portion of the co-enzyme nucleus is supplied exogenously. Thus, niacinamide hydrobromide represents a safety factor in tranquilizing bromide medication.

Since the original study(1) of 50 cases, comparing the use of plain triple bromides with the niacinamide hydrobromide combination, 440 cases have been added to series. Statistics show that some manifestation of untoward effect has been present in approximately 15% of the cases. True bromism has been demonstrated in approximately 4% of the cases. The total figure of 15% has been reduced to less than 2% with the use of the niacinamide hydrobromide combination.

A typical case study was that of a married woman, age 28, who was treated alternately with bromides and phenobarbital for relief of extreme nervous tension. In response to either medication the patient exhibited an acneform rash covering the whole body and causing pruritus at multiple sites. When the medication was withdrawn, the rash disappeared. It was found that the niacinamide combination with ammonium and potassium bromides prolonged the therapeutic effect and also prevented the rapid development of the untoward response.

[1] 150 Woodruff Ave., Brooklyn 26, N. Y.

[2] Natran tablets containing ammonium bromide 250 mg., potassium bromide 250 mg. and niacinamide hydrobromide 10 mg. supplied by the John Winters Co., 313 East 53rd St., New York 22, N. Y.

The appearance of pellagra-like symptoms with rapid clearing when the co-enzyme pyridine nucleus was supplied demonstrates clinically the mechanism of interference with the enzyme oxidation mechanism of the body economy by such substances as phenobarbital and bromide. Other newer types of sedatives gave similar results.

In summary, clinical and laboratory evidence suggests that tranquilizers, including the bromides, can interfere with the co-enzyme system causing the pellagra-like syndrome. There has been abundant clinical evidence that these symptoms are reversed in 87% of cases and the response has been to clear up 50% of the small group exhibiting actual bromism, when the combination of ammonium and potassium bromides with niacinamide hydrobromide as a safety factor has been used as a tranquilizer.

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INPATIENT TREATMENT OF DEPRESSIVE STATES WITH TOFRANIL (IMIPRAMINE HYDROCHLORIDE)[1]

W. KEUP, M.D., A. APOLITO, M.D., L. OLINGER, M.D., M. SCHWARTZ, M.D., AND E. YACHNES, M.D.[2]

In 1957 Kuhn(1) published his first results with the new anti-depressive drug Tofranil[3] (G-22355, imipramine hydrochloride), which turned out to have no monoamine oxidase (MAO) inhibiting effect, in contrast to iproniazid and its new and less toxic followers. Differences in the clinical actions of Tofranil and the MAO inhibitors are supposed but not sufficiently elaborated.

As a first step we therefore studied the action of Tofranil alone in a series of 66 hospitalized unselected depressed patients with different diagnoses, 28 male and 38 female, whose ages varied between 25 and 72 years. The majority of the depressions were endogenous (28 involutional, 11 manic depressive), while 17 schizophrenic patients with depressive features and 10 patients with arteriosclerotic, senile or psychoneurotic depressions were also included. About one-third of all these cases were chronically depressed patients, some of whom had received ECT, insulin therapy, and different tranquilizing drugs without effect.

The drug was given by oral administration only, starting usually with a dosage of 75 mg. per day which was increased slowly to a mean dosage of about 200 mg. per day, adjusted individually. In some cases higher doses up to 400 mg. per day were used. It is believed that prolonged treatment with a low maintenance dosage is necessary to prevent relapses(2, 3). We used long term treatment, up to 5 months.

Best results were seen in endogenous depression, confirming findings of other authors(1, 4, 5). In this group, 10 patients (26%) recovered, 22 (56%) showed moderate to good improvement and 7 were unchanged. Schizophrenic patients did not respond as well, 10 remaining unchanged and 7 showing moderate or good improvement. The mixed group was also less responsive with 4 patients out of 10 showing some degree of improvement. The overall results showed that 65% of all patients treated manifested some degree of favorable response, with 17% total recovery. While these figures are lower than those reported by some previous investigators(4), the improvement rate in our cases of endogenous depression, 80%, is quite in line

[1] Preliminary note on a paper read at the Downstate Interhospital Conference, New York, April 6, 1959. Will be printed in full in J. Nerv. Ment. Dis.

[2] Brooklyn State Hospital, Brooklyn 3, N. Y.

[3] Kindly supplied for this study by Geigy Pharmaceuticals, Ardsley, New York.

with previously reported data.

From the standpoint of symptoms affected, best improvement was seen in affective depression, flow of psychological activity and alteration of thought process. Some patients showing overall improvement in the depressive state, nevertheless had worsening of one or two symptoms. In 9 patients impending or manifest agitation was observed, mainly with higher doses. In 8 of these patients, this agitation was controlled by administration of a tranquilizing drug (Thorazine, reserpine).

Other side effects observed were minor and consisted of dizziness, 3 patients, nausea, 1, blurred vision, 2, perspiration, 2, dry mouth, 2, and constipation, 2. A slight drop in blood pressure was observed in a few patients, but in some of our elderly patients this was actually a desirable side effect but not a constant one. Some of these side effects were seen only during the onset of treatment and disappeared as therapy continued. This was true for a slight tremor of the hands in 6 patients, but we observed no other extrapyramidal symptoms.

Improvement can be observed as soon as the first or second day in some patients, but sometimes it takes 2 or 3 weeks. According to our experience, the patient who does not respond during the first 3 weeks, will not respond at all.

From the above we can conclude that Tofranil is the most potent antidepressive drug available at the present time, comparable in affectiveness with electro-shock therapy. While ECT may still be preferred in acute suicidal patients, it is our impression that this drug reduces the need for ECT drastically.

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NEGATIVE RESULTS IN THE TREATMENT OF DEPRESSION WITH IMIPRAMINE HYDROCHLORIDE (TOFRANIL)

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A number of reports from Europe and several from America have been enthusiastic regarding the effectiveness of imipramine hydrochloride (Tofranil, Geigy Pharmaceuticals) in the treatment of depression. My own experience with this drug in 137 private patients over a 2 year period has been disappointing. These were all cases in which depression was the most prominent symptom and most of them were of the endogenous type.

The dosage used was from one to two 25 mg. capsules q.i.d. for 3 or 4 weeks provided the patient could be persuaded to take the medicine that long. The size and duration of medication were frequently limited by unpleasant side effects or failure of beneficial results. None of the side effects was serious but dizziness, dry mouth, blurred vision, increased tension and perspiration often caused the patients to discontinue this drug.

Only 22 of the 137 thought that imipramine was of help and their initial enthusiasm usually waned as the medication was continued. No patient has asked to or was interested in continuing this drug beyond the first trial month. The evaluation of the pharmacological treatment of depression is especially difficult because most of these cases are self limited anyway and whatever is being given at the time of recovery is credited with the cure. This is especially

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true where it is recommended that the drug be given for at least a month before judging its effect.

In view of reports of success with this drug by others, it would seem advisable to continue clinical trials, especially control studies, but my own experience so far has been disappointing.

A MODIFICATION OF THE FORREST TEST FOR PHENOTHIAZINES

JACK J. HEYMAN, M.S., M. ALMUDEVAR, M.D., AND SIDNEY MERLIS, M.D.[1]

The routine determination of phenothiazines in urine samples has been thoroughly investigated by Forrest(1-2) and separately by Pollack(3). In our laboratory we modified the procedure to obtain more stable color development and at the same time preserve the simplicity of the Forrest method.

MATERIALS

A sulfonic acid resin impregnated paper SA-1 or SA-2[2] was further prepared by immersing strips 7″ x ¾″ in filtered 2% ferric chloride solution (2g $FeCl_3$/100 ml. H_2O). The paper was blotted dry with clean paper towelling and oven-dried at 80° C. The prepared paper is stable.

METHODS

A drop of urine from a morning sample was placed on the paper and one drop of 15% sulfuric acid placed in the center of the ring formed by the sample drop. A violet colored ring develops in the presence of metabolized phenothiazine. The color intensity observed is constant in intensity for each individual patient on a constant drug intake. The drug intake can be graded (Table 1) by the intensity of color observed

TABLE 1

GRADING OF THE RESULT

Grade	*Dose In Mg./Day/Pat.*	*Color*
0	0-50	yellow
plus/minus	50-75	faint pink
1 plus	50-100	violet or red
2 plus	150-600	dark violet or red
3 plus	600-900	very dark violet or red
4 plus	Overdose	extremely intense, one or more rings, violet and red.

or by diluting the sample with distilled water and testing a 1:1 serial dilution. The last positive tube number is recorded for the particular patient at the dose given. If the dose is changed, the color intensity changes, and the number of positive tubes change.

The same procedure can also be used as a toxicological aid. With gastric juice the unmetabolized phenothiazines give red coloration while the urine will show an intense violet, red or both colors. By making a serial dilution, the quantity present can be estimated (Table 2).

Running the same dilutions with a known phenothiazine until a negative result is

TABLE 2

DILUTIONS OF SPECIMENS

Tube #	*0*	*1*	*2*	*3*
ml. of Sample	1 ml. urine or gastric juice	1 ml. urine or gastric juice	1 ml. of #1	1 ml. of #2
ml. of Diluent	———	1 ml. of H_2O	1 ml. of H_2O	1 ml. of H_2O
Fraction of original Concentration	1	½	¼	⅛

[1] From the clinical facilities and research laboratory of the Research Division, Central Islip State Hospital, Central Islip, N. Y.

[2] The ion-exchange paper was supplied through the courtesy of H. Reeve Angel & Co., Inc., 52 Duane St., New York, N. Y.

obtained gives the "approximate minimum detectable quantity" (AMD). Several observed values are listed as follows :

Drug	AMD mg./ml.
Thorazine	.031
Sparine	.015
Compazine	.031
Vesprin	.031
Pacatal	.031

The approximate amount present is calculated by the equation :

2^n x AMD=quantity present.

Where n=# of the tube in 1:1 dilution series

AMD=Approximate minimum detectable quantity.

Conclusions

This test has several advantages over the Forrest Method. The color developed is fairly stable, with only slight fading observed in 24 hours. As little as one drop of sample is sufficient for grading the quantity of phenothiazine present. Therefore, the test can be used with samples from incontinent patients. A close estimation of overdoses can be made. The test retains the good qualities of the Forrest Method : it is rapid, sensitive and does not give false positives. All the phenothiazines tested gave positive results when the dose level was above 50 mg. daily.

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AMINO-GLUTETHIMIDE IN THE TREATMENT OF CHRONIC PSYCHOTIC EPILEPTICS

G. DONALD NISWANDER, M.D. AND ISMET KARACAN, M.D. [1]

A glutarimide derivative, glutethimide, known for its sedative properties, was observed to have an additional anti-convulsant activity when used in the treatment of epileptic patients(1). Consequently, attempts were made to find other glutarimides with anti-convulsant activity, but without sedative effects. A compound, known chemically as a-(p-amino-phenyl)-a-ethyl glutarimide, hereafter referred to as amino-glutethimide,[2] was discovered to have a good anti-convulsant activity without the sedative side effect.

Lambros has previously reported his experience with amino-glutethimide in a group of epileptics treated as outpatients (2). Eighty per cent of Lambros' patients improved, in terms of a decrease in number of seizures while receiving the medication. Sheehan has mentioned his experience with this compound, but he does not give results obtained with it(3).

Below are the results of 9 months experience and observations in the use of amino-glutethimide for the treatment of chronic hospitalized psychotic epileptic patients.

METHOD OF STUDY

Twenty-five female and 13 male patients were selected on the basis of the diagnosis "chronic brain syndrome associated with convulsive disorder, with psychotic reaction." Age range was from 25 to 76 years, with a median age of 40 years. The duration of hospitalization extended from 4 to 35 years, with a median duration of 10 years. Each of the patients was receiving either phenobarbital or diphenylhydantoin alone or in combination previous to the study. Initially each patient was given either 125 mgs. or 250 mgs. of amino-glutethimide daily. This dosage was increased by this same amount every 5 days until a therapeutic level of the drug was reached of between 750-2,000 mgs. daily. When amino-

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[2] The amino-glutethimide used in this study was supplied as Elipten by the Ciba Pharmaceutical Products, Inc., Summit, N. J.

glutethimide was prescribed, the other anti-convulsants were gradually withdrawn over a 4 week period. Blood pressures, blood counts, and urinalyses were evaluated periodically during the study. Grand mal seizure frequency had been carefully recorded before the study, and this was continued during the experiment.

RESULTS

The withdrawal of previous anti-convulsant medications after prescribing amino-glutethimide was successfully carried out in all but one female patient, who developed status epilepticus. After this condition was controlled, the compound, in combination with the previous medication, was re-prescribed resulting in fewer seizures. In other patients who had more seizures, the diphenylhydantoin sodium and/or phenobarbital sodium were re-prescribed in reduced dosage levels with better seizure control.

In regard to control of grand-mal seizure frequency, amino-glutethimide is an effective anti-convulsive medication, used either alone or in combination with other anti-convulsants.

In the last 5 months of the study, after stabilization of this epileptic group, grand-mal seizures were reduced 25-35% compared to seizure frequency before the project began.

At the beginning of the study, 2 patients (5.3%) developed a macular rash which was more prominent on the extremities. The rash disappeared within 4 days after the medication was discontinued. Each of these patients had begun receiving 250 mgs. of the compound daily, which had been increased 250 mgs. on the fifth day. None of the patients who initially started on the smaller dosage of 125 mgs. developed a rash. In view of this observation, patients added to the study thereafter were started on the smaller dosage; no further skin reactions have occurred.

Two patients receiving 1,500 mgs. of amino-glutethimide daily complained of nausea. Two patients receiving this amount of the drug were observed to have a staggering gait and unsteadiness while standing. When the dosage was reduced to 750 mgs. all of these symptoms subsided. These side effects from amino-glutethimide observed in this study are in accordance with what other investigators have reported. Drowsiness was not observed as a side effect. No significant changes were found in blood pressures, urinalyses, and blood counts.

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CHEMOTHERAPEUTIC TRIALS IN PSYCHOSIS: III. ADDENDUM
2-Brom-d-Lysergic Acid Diethylamide (BOL)

WM. J. TURNER, M.D., MANUEL ALMUDEVAR, M.D., AND SIDNEY MERLIS, M.D.[1]

In a previous communication(1) we have reported: "BOL-148 administered to chronic schizophrenics, 1 mg. t.i.d. to 6 subjects for 2 weeks, or 5 mg. q.i.d. for 3 days to 3 subjects, had no evident effect on their psychoses." Subsequently the work of Schneckloth, Page, del Greco and Corcoran(2) led us to consider whether we had used doses too small to demonstrate any therapeutic action. Accordingly, 6 schizophrenic women were included in a further study. These patients had been on our Research Ward for periods up to 18 months. With each of them we had excellent rapport, and the transference reactions of dependency, and their expectation that they would be saved was quite clear. Three of them were known to be hallucinating most of the time. All had extreme feelings of guilt and were withdrawn except under favorable situations, with a person to whom they had become attached.

Each subject received a dose of LSD, 75 gamma, preceding the start of BOL

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medication. The LSD clearly brought out in each instance a psychic disturbance, with agitation, anxiety with exacerbation of the helpless dependency needs, or defensive hostility. Their experiences were described in such terms as "inability to stop memories," "something happening to me," or : "What was in that glass ? I can't think right."

All patients were started on 10 mg. of BOL 3 times a day.[2] One patient had such a degree of alarm and agitation on this dose that she was reduced to 1 mg. daily for the first week. Several of the other patients commented on the fact that the first morning dose made them feel very jumpy and rather fearful that they might break down, for instance, from a "cool, distant reserve." Medication continued for a minimum of 4 weeks ; 2 patients continued for 5 weeks. On their last day 4 of the patients received 1 mg. of BOL plus 150 or 200 gamma of LSD. The other 2 patients had no BOL for 18 hours preceding LSD 150 gamma and 200 gamma respectively. In all 6 instances the response to LSD was completely absent.

Interviews, observations of behavior and subsequent descriptions by 4 of the patients confirmed our impression that no change in attitude had taken place under the action of BOL. Hallucinations, when present before, were of the same intensity and quality at the end of the BOL experience. Hostile aloofness, anxiety, withdrawal, feelings of hopelessness, of injustice, of ultimate submissiveness, of bewilderment and perplexity, all remained unchanged.

COMMENT

The work here reported is part of our effort to clarify and if possible to define the role of biochemical factors in the pathogenesis of schizophrenias. One aspect of this is a widely accepted assertion that LSD produces a "model psychosis," a model, so to speak, of schizophrenia. In the face of the data which have been published in support of this assertion our limited data and personal experiences must carry little weight but, for what it is worth, we do not agree. Some of our reasons have been stated by or are implicit in the data of other workers (Hoch(4), Levin(5), Stoll(6), Bleuler(7)). To these we would add one not previously reported, to our knowledge : our patients who were able to communicate told us that the LSD experience was not the same as their psychotic experience.

It might be objected that we have not shown conclusively that the LSD reaction was completely blocked. The difficulties in doing a formal study of psychotic subjects under LSD are well known. The rarity with which the psychotic subject reports the visual disturbances which play so prominent a part in the reaction of non-psychotic subjects is also well known. When these difficulties are combined, we feel that the best means of testing the LSD reaction is to compare one patient with herself at different times. Since we have done this, we believe that we are justified in claiming that the reaction to as much as 200 gamma of LSD was completely blocked by BOL. It is of theoretical importance that the abolition of the LSD reaction may occur without interfering with the patient's pre-existing psychosis.

[2] The BOL tablets were provided through the courtesy of Dr. R. Bircher of Sandoz Pharmaceuticals.

SUMMARY AND CONCLUSIONS

BOL in doses of 10 mg. orally 3 times daily for 4 to 5 weeks was administered to 6 chronically ill schizophrenic women. This abolished the response to LSD up to 200 gamma but failed to alter the psychosis in any way. Initial doses of 10 mg. BOL may produce mild LSD-like reactions.

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COMMENT

STATISTICS AND STATISTICIANS: A TIMELY WARNING

WERNER TUTEUR, M.D.[1]

Scientific claims should be judged on experimental evidence rather than on plausibility and conformity, Hopkins warned recently. He added that the practitioner of psychiatry is leaning on a weak reed if he depends merely on the findings of specialized research workers. Psychiatric research, he states, is starving to death for want of ideas, space, mature and well trained personnel(1).

Statistics, euphemistically considered reliable sources of information, may at times be confirming, confusing or misleading. New methods of treatment usually are evaluated with "true statistical facts," allegedly proving the point in question. Frequently one is deluged by numerical data of clinical studies, most of them, no doubt, representing well motivated and honest work, many showing the most sophisticated and elaborate detail. At such occasions one does well to remember some examples of basic fallacies inherent in statistics and statisticians. They show how loosely certain concepts can be used and the false security on which conclusions are sometimes based.

For many decades it has become a popular slogan that every other hospital bed in the United States is occupied by a mental patient. This is perfectly true for a given day in the calendar year, but it does not mean that mental illness prevails among half of all hospitalized patients. Many are the times when one hears this "every other bed" slogan during campaigns, lectures and addresses by lay persons as well as those belonging to our ranks. The fact is frequently overlooked that the same general hospital bed is used throughout the year by a large number of patients with physical illness, that the general hospital turnover in no way compares with that of a mental hospital and that thus the general distribution of morbidity is entirely removed from the fact that "half of all hospital patients are mental cases."

Per diem rates prevailing in State and Government operated institutions are a favorite subject regarding "better care for the mentally ill." Easily the conclusion is reached by the uncritical that the agency showing the highest *per diem* rate gives the best and the one with the lowest, the worst, care to its patients. Completely overlooked is usually the fact that *per diem* rates by necessity are derived from the most varying basic circumstances. At the Ninth Mental Hospital Institute held at Cleveland, Ohio, this subject created a lively discussion headed by Blasko(2). Among many other issues the following highlighted the debate. States located in moderate climates spend little on fuel, while those exposed to inclement weather sometimes do so in excess. Food prices vary from state to state and are to a large measure dependent on the market value of home grown products, rendering the *per diem* rate low. Union wages for crafts vary across the entire country, once more introducing a variable into the *per diem* rate which has absolutely no bearing on psychiatric care.

Much inaccuracy prevails statistically on the matter of suicides. The drop of suicides during wartime is allegedly an "established fact." Evidence shows that this is erroneous. Raines speaks of concealed suicides occurring in the Armed Forces during war(3). The unaccounted number and the unknown motivations of men volunteering for dangerous missions, almost always representing a great risk of death and ending fatally, falls into this category. Or, soldiers landing on a beachhead walking into a mine field and promptly being blown apart, ignoring warning signs "as large as box cars," likewise seem to indicate successful suicidal attempts never covered statistically.

The very interesting phenomenon of physiological suicide(3) escapes statistical evaluation completely. Here belong hitherto well balanced diabetics who wilfully become unmanageable, slip into coma or

[1] Clinical Director, Elgin State Hospital, Elgin, Ill.

shock to die, cardiovascular patients who discontinue their medicinal regimen and become otherwise uncooperative with the overt or covert wish to die, and many others.

These are only a few examples of statistical looseness, of poorly disciplined and faulty thinking, leading to erroneous conclusions. Such thinking makes for scientific detours, for inaccuracy, of which psychiatry is replete already, since human data *per se* are qualitative, frequently sparse and mostly subjective. To this should be added the physiological margin of error inherent in most clinical work, rarely mentioned publicly, for which allowance is hardly ever made. Only after diligent filtering will statistics—without which we could not do—avail themselves for proper interpretation.

"I respect faith, but it is doubt that gets you an education" was said once by Wilson Mizner.

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EDUCATION

Education, in short, cannot be better described than by calling it *the organization of acquired habits of conduct and tendencies to behavior.*

—WILLIAM JAMES

VERITAS

Marxism a science ? I don't know a movement more self-centered and further removed from the facts than Marxism. Every one is worried only about proving himself in practical matters, and as for the men in power, they are so anxious to establish the myth of their infallibility that they do their utmost to ignore the truth.

—PASTERNAK
(Dr. Zhivago)

CORRESPONDENCE

DR. SAMUEL W. HAMILTON AND THE FOUNDING OF THE AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY, INC.

Editor, THE AMERICAN JOURNAL OF PSYCHIATRY :

SIR : In the March issue of the American Journal of Psychiatry I was interested in reading the article on "The Founding of the American Board of Psychiatry and Neurology," established as a result of the conference held under the auspices of the Division of Psychiatric Education of The National Committee for Mental Hygiene, Inc. (now The National Association for Mental Health, Inc.).

There is one name missing among those credited with the preparatory work of this Board, and if the authors (and the readers, too) were not aware of his participation it was due, I am sure, to his self-effacement. That person was the late Dr. Samuel W. Hamilton.

In 1933 at the time preparations were being made to call this conference, Dr. Hamilton was the Acting Director of the Division of Psychiatric Education of The National Committee for Mental Hygiene. It was he who gathered the directories of the medical specialty boards then in existence as samples and prepared the materials used in the discussions at the Boston conference in May, 1933. It was he, too, who made the arrangements for this conference and invited the participants.

Perhaps one should mention also, in this connection, the late Paul O. Komora (Assistant Secretary of The National Committee for Mental Hygiene), who for 25 years worked closely with the American Psychiatric Association on various projects and was present at the first conference on psychiatric education, at which the desirability of the establishment of a specialty board in psychiatry and neurology was discussed. To Mr. Komora we are indebted for the excellent report of that meeting which is listed in the references at the end of the article "The Founding of the American Board of Psychiatry and Neurology."

Emily L. Martin,
(formerly Executive Secretary,
Division of Psychiatry Education,
The National Committee for
Mental Hygiene, Inc.)

REPLY TO THE FOREGOING

Editor, THE AMERICAN JOURNAL OF PSYCHIATRY :

SIR : On behalf of my co-authors I wish to make amends for the oversight in omitting the name of Dr. Samuel W. Hamilton from those who contributed to the founding of the American Board of Psychiatry and Neurology.

None of us attended the important Conference on Psychiatric Education May 28 and 29, 1933, but Dr. Hamilton's remarks upon that occasion brought the whole problem into focus. We are gratified that Miss Martin has brought Dr. Hamilton's contribution to the notice of both ourselves and of the readers of the American Journal of Psychiatry.

Walter Freeman, M.D.,
Los Altos, Calif.

HYPERTENSION DUE TO CHLORPROMAZINE

Editor, THE AMERICAN JOURNAL OF PSYCHIATRY :

SIR : With reference to the case report entitled "Prolonged Hypotension due to Chlorpromazine" by Dr. W. J. Stanley, in the June 1959 issue of The American Journal of Psychiatry, I believe that another blood pressure reaction related to chlorpromazine treatment should be looked for because of its possible hazards. This reaction is hypertension following administration of chlorpromazine.

Dr. Nathan Beckenstein, Director of the Brooklyn State Hospital, informed me that a drastic rise in blood pressure has occurred in young, ordinarily normotensive, male patients approximately 4 hours subsequent to an intramuscular injection of as little as 50 mgm. of chlorpromazine. This apparent withdrawal type response was noted in studies done at the Brooklyn State Hospital some time ago.

Recently I have had occasion to treat a 62-year-old white married man with chlorpromazine by mouth for an involutional psychotic reaction. This patient had a coronary occlusion several years before, had been a known hypertensive, and had suffered from angina pectoris until approximately 3 years prior to my seeing him. After he had improved considerably from psychotic symptoms, chlorpromazine (50 mgm. q.i.d.) was discontinued. Within the 24-hour period following, the patient became nauseated, and EKG showed recurrence of an arrythmia. The internist who treated him reports that the patient was again placed on chlorpromazine with improvement of nausea and cardiac symptoms.

Dr. Beckenstein's experience, and mine with this patient, suggest that subsequent to the administration of chlorpromazine, a pronounced hypertension may occur which could be disastrous to those with preexistent cardiovascular disease.

The purpose of this letter is to call this to the attention of those who may have similar observations or who desire to investigate the cardiovascular effects of chlorpromazine withdrawal.

Edward L. Pinney, Jr., M.D.,
Brooklyn, N. Y.

STYLE

Cultivate simplicity, Coleridge, or rather, I should say, banish elaborations ; for simplicity springs spontaneous from the heart, and carries into daylight its own modest buds and genuine, sweet, and dear flowers of expression.

—CHARLES LAMB
(in a letter to Coleridge Nov. 8, 1796.)

MATHEMATICS AND REALITY

In my opinion the answer to this question is briefly this : as far as the laws of mathematics refer to reality, they are not certain ; and as far as they are certain, they do not refer to reality.

—EINSTEIN

HISTORICAL NOTES

BI-CENTENARY OF THE BIRTH OF VINCENZO CHIARUGI (1749-1820) A PIONEER OF THE MODERN MENTAL HOSPITAL TREATMENT

GEORGE MORA, M.D.[1]

The picture of psychiatry at the beginning of the 19th century, as described by Kraepelin in a little remembered, but significant book,[2] is very important. The verbal description and the pictorial reproduction of the methods of treatment in use at that time—from cruel strait jackets and other torture-like devises to isolation in filthy cells, from rotatory machines to complicated systems of sudden baths—leaves one today with a feeling of disgust and sadness. Yet, these methods were in use only a century and a half ago—and they had to continue through the first decades on the 19th century—at the time when a long tradition of Christian ethics and a more recent one of scientific progress had established their strongest roots in the Western European thought.

At the height of the Enlightenment, centuries after the fore-running modern viewpoint on treatment of mental patients as expressed by Aretaeus and Soranus[3]—not to mention the Arabian humanitarian approach and the "Renaissance" psychiatry of Weyer[4]—at the time of the greatest enthusiasm for human knowledge, not only in the scientific but also in the "humanistic" fields, from medicine to sociology and jurisprudence, the general attitude toward mental patients was still characterized by mistrust, suspicion, horror, and cruelty. Others[5] have attempted to clarify this unconscious fear toward mental patients, which accounts for such an irrational attitude, a fear which seems almost paradoxical at the time when rationalism prevailed.

Certainly, no matter how strong these prejudices dictated by fears must have been, some signs, harbinger of a new approach to mental diseases, were already present. The importance of "passions" for the understanding of human psychology, a concept introduced by Descartes in 1649, started to appear in some of the most important writings of physicians of the time,

[1] Director, Out-Patient Department, Bradley Hospital, East Providence, R. I.; Research Assistant, Department of the History of Medicine, Yale School of Medicine.

[2] E. Kraepelin: Hundert Jahre Psychiatrie, Berlin: Springer, 1918. Kraepelin summarizes the situation of psychiatry at the beginning of the 19th century in these terms: "Disregard for and crude treatment of the mentally sick, lack of appropriate physical facilities and medical care, uncertain and strange ideas on the causes and essence of insanity, torture of patients through meaningless and at times extravagant means of treatment. It would certainly be unfair to expect that the above mentioned factors could result in progressive developments. It is true that then and even earlier there were individual places in which patients were treated well and properly. There were even physicians who achieved a better understanding of mental disturbances by their rich experience and natural ability and who, endowed with a serene viewpoint and a warm approach, followed the right direction in the treatment of their patients. These exceptions alone, however, could not decisively influence the general state of scientific knowledge and the destiny of large masses. They were only the seeds, from which, under the most favourable circumstances, the science of psychiatry could develop in the following century." (p. 68)

[3] Aretaeus and Soranus, both active in medicine toward the end of the first century A.D., introduced a very humanitarian approach in the treatment of mental diseases, as related by Caelius Aurelianus in his works *On Acute Diseases* and *On Chronic Diseases* (5th century A.D.).

[4] Johann Weyer, or Wier (1515-1588), the most well known among a number of authors who fought the belief in witchcraft in the late 16th and early 17th centuries, wrote the important book *De prestigiis daemonum* in 1563. He is currently considered as the first pioneer of psychiatry. The humanitarian approach to mental diseases, as applied in some islamic countries around the 15th century, still remains largely unknown today. It contains many elements, however, similar to those pursued by modern psychiatry, as can be seen in the recent study by J. E. Stahelin: Zur Geschichte der Psychiatrie des Islams, Schweiz. med. Wchnschr., 87: 1152, 1957.

[5] G. Zilboorg, A History of Medical Psychology, New York: Norton, 1941, passim; A. Gregg: A critique of psychiatry, Am. J. Psychiatr., 101: 285, 1944.

from George Stahl (1702) to Boissier de Sauvages (1771) and Clement Tissot (1798).[6] Parallel to a timid pre-romantic trend in the 18th century philosophy and literature, an initial trend toward a more comprehensive attitude toward human beings, even in their irrational expressions, began to manifest itself sporadically in the vast, and cold, nosographic structures of medical writers.[7] The synthetic effort evident in the all-comprehensive medical and philosophical systems of the 18th century could not completely overshadow a genuine interest for the individual and his problems.

This trend was also present in psychiatry, where some isolated individuals—under the influence of the English philosophy and of the French Enlightenment—started to question the validity of the cruel treatment to mental patients. While the need for reforming the treatment to mental patients was strongly expressed by Jacques Tenon (1788) and by Jean Colombier (1789), a more humanitarian, but still pre-scientific approach toward mental diseases was already applied at the Charité de Senlis in Paris,[8] as well as in similar places. So far, however, official medicine had remained absent from this movement. Strangely enough, the first decisive step toward a scientific reform in psychiatry occurred in Italy, a less progressive and "enlightened" country than France and England.

The evaluation of the cultural situation of the 18th century European countries is a matter of recent investigation, as such an evaluation has been traditionally limited to France and England. The general characteristics of Italian Enlightenment, essentially an integration of the cultural movement by the political absolutistic element with emphasis on concrete and practical aspects, have been brought into focus only recently. Of the several states in which Italy was divided in the second half of the 18th century, these renewing currents were especially evident in Lombardy in the field of public administration, in the kingdom of Naples in the field of jurisprudence and economy, and in Tuscany in the field of politics and social welfare. It is especially to the cultural scene of Tuscany during the rule of the Grand Duke Pietro Leopoldo (1747-1792), that modern historians have turned their attention. The importance of the series of reforms affecting all the areas of the state's life, economic, financial, judicial, educational and social during his 25 years of ruling, from 1765 to 1790, have been emphasized by many.

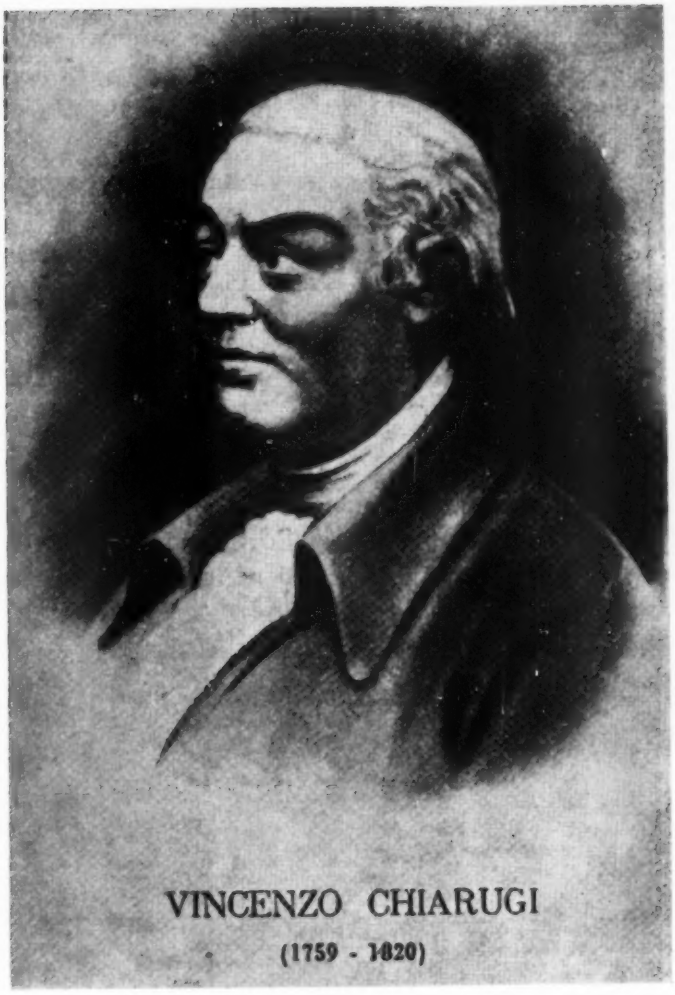
A chemist himself, Leopold was a fervent admirer of the social ideas brought to Italy by the English and French Enlightenment. He introduced the *Encyclopédie* in Italy in 1758, permitted the publication of important social and legal works (such as Cesare Beccaris's *On Crime and Punishment*),[9] and surrounded himself with scientists and skillful physicians who brought reputation to the universities of Pisa and Florence, in line with the tradition inaugurated by Galileo two centuries before. As a completion of such an important program of reforms, the Grand Duke Leopold and his collaborators elaborated in detail a project for a political constitution—similar in its general philosophy to the first Constitution of Virginia of 1776—which unfortunately could not be put into effect because of the departure of the Grand Duke for Vienna to become emperor in 1790. Even admitting that such a project was far above the capacity of comprehension of the population so to raise opposition rather than support, the judgment of the historians is unanimous in indicating in Pietro Leopoldo the most progressive ruler that Italy ever had and in his peaceful reforms the application of the democratic principles which had to wait for 30 years more —after the horrors of the French revolu-

[6] George Stahl (1660-1734), Boissier de Sauvages (1706-1767) and Clément Tissot (1750-1826), well known physicians of their time, all emphasized the influence of emotions on mental and physical diseases, anticipating many views presented later.

[7] Among the attempts to classify physical as well as mental diseases in a comprehensive system, the most important remain those by Boissier de Sauvages (*Nosologie methodique*, 1771), by William Cullen (*First Lines of the Practice of Physick*, 1777 and *Treatise of the Materia Medica*, 1789), and by Erasmus Darwin (*Zoonomia*, 1794).

[8] H. Bonnafous-Sérieux: La Charité de Senlis, Paris, Presses Univ. de France, 1936.

[9] Cesare Beccaria (1738-1794) acquired an international renown through his work *On Crime and Punishment* (1764), translated in many languages, in which he made a plea for moderating punishments and for abolishing confiscation, torture and capital punishment.



VINCENZO CHIARUGI

(1759 - 1820)

tion—to be finally formulated in the French constitution.

Among the decisions taken by the Grand Duke were the abolition of the torture and death penalty for severe offenses, which culminated in the public destruction of the torture tools in 1782, and the foundation of a special institution for the rehabilitation of juvenile delinquents. An event even more important than these, but unfortunately almost universally overlooked by historians, is the foundation of the Hospital Bonifacio in Florence in 1788, entirely dedicated to the care and treatment of about 125 mental patients.

Vincenzo Chiarugi, a brilliant young physician, born near Florence in 1759, and graduated from Pisa in 1780, was put in charge of this new hospital. The following year, 1789, Chiarugi published the *Regulations of the Hospital Bonifacio,* which contain the foundations for the treatment of mental patients and which anticipated the philosophy of "moral treatment" of the following decades in Europe as well as in this country.[10] On the basis of the experience accumulated in some years of intensive work at the hospital, Chiarugi published in 1793-1794 his main work, in 3 volumes, *On Insanity,* which constitutes today a very rare bibliographical item.[11] Following this, in 1802, he was appointed professor of dermatology and mental diseases at the newly established medical school of Florence, and later on he became professor of physiology, pathology and materia medica. He died in 1820.

In his work *On Insanity* Chiarugi makes a strong plea against the old belief concerning mental diseases as due to possession by evil spirits and tries to base his statements only on scientific observations. The *psychological foundations of the individual* are still largely based on a combination of Aristotelian-tomistic philosophy with cartesianism, a view which he supports by following many students of the nervous system of the 16th and 17th centuries. In spite of the fact that passions are given importance ("between passions and insanity there is only a difference of degree and duration"), he considers insanity as an "impairment of the physical structure of the brain." As a true follower of Morgagni, each case described contains a summary of the history, of the clinical manifestations and at times of the pathological findings.

He presents a *division of insanity in three major categories*: (a) melancholia (b) mania (c) amentia, a classification which was essentially followed in other books, including Pinel's treatise. *Melancholia* (true, false, or violent) is characterized by "fixation of the mind on one or a few distorted ideas, while the other intellectual functions remain untouched." *Mania* is "a generalized insanity accompanied by violent and impetuous actions." *Dementia* (congenital or acquired) "is general insanity characterized by abnormal actions of both the intellect and the will, performed without any show of emotions."

Many factors both congenital and acquired are considered either as predisposing or precipitating *causes* of insanity, but large emphasis is also given to environmental factors. "As man's natural disposition is to imitate the actions of his associates, through education a man's character is molded, his senses develop and even his inclinations may be modified."

As far as *diagnosis* is concerned, "in describing the nature of insanity in general, one must first have an idea of what the essential elements are and consider the external signs and the general phenomena which accompany it." And later "there is a considerable change in the instincts and personality of a mentally ill person." Furthermore, he emphasizes the value of a careful description of the physical and emotional aspects of the patient's personality, and insists on the manic-depressive course of many psychiatric conditions.

In discussing *prognosis,* he states that

[10] According to the historian Antonio Zobi (*Storia civile della Toscana,* Firenze, Molini, 1850, vol. 2, p. 324) these *Regulations* served as an example to improve the condition of other mental hospitals in different countries.

[11] The full title of this work is: *Della pazzia in genere e in specie con una centuria di osservazioni* (*Medical Treatise on Insanity, with one hundred observations*), Firenze, Carlieri, 1793-1794, 3 vols.; 2nd. ed. Firenze, Pagani, 1808. This work soon appeared in German under the title: Abhandlung ueber den Wahnsinn ueberhaupt und insbesondere nebst einer Zenturie von Beobachtungen, Leipzig, 1795. Only 2 copies of the original Italian first edition are known in this country, one at the National Library in Cleveland and the other at the Yale Medical Library.

long term conditions, especially if combined with badly regulated education, have a more unfavorable outcome than conditions due to acute or physical causes.

Chiarugi's main contribution to psychiatry remains, however, in the treatment of mental diseases. After mentioning the importance of diet, of drugs, and the favourable effects of music on certain conditions, Chiarugi formulated in detail the *principles of hospital care and treatment* both in the "Regulations of the Hospital Bonifacio" and later on in his book *On Insanity*. These are the main points of his philosophy: Patients are to be admitted to the hospital only after a careful history has been obtained; a physician has to be on duty in the hospital at all times; under no circumstance should force be used on patients; temporary restriction methods are limited to the use of strait jackets and strips of reinforced cotton cloth, so as not to intefere with the patient's blood circulation; special precautions are to be taken in regard to furniture and other supplies, so as to prevent injuries; the hygienic conditions of the institution have to conform to certain basic requirements; activities for patients are to be encouraged, though only under the supervision of the physician.

As far as direct or "moral" treatment is concerned:

> It is a supreme moral duty and medical obligation to respect the insane individual as a person. It is especially necessary for the person who treats the mental patient to gain his confidence and trust. It is best, therefore, to be tactful and understanding and to try to lead the patient to the truth and to instill reason into him little by little, in a kind way.

Later on:

> The attitude of nurses and doctors must be authoritative and impressive, but at the same time pleasant and adapted to the impaired mind of the patient. Generally, it is better to follow the patient's inclinations and give him as many comforts as is advisable from a medical and practical standpoint.

Clearly as results from the above mentioned, Chiarugi anticipated both in theory and practice the scientific views and the reform later introduced by Pinel and his followers in the field of mental diseases.[12] A striking similarity in both precursors, Chiarugi and Pinel, is indicated by the fact that their reforms of the treatment of mental patients could succeed only in an atmosphere of social progress and of political freedom, such as in Tuscany in the late 18th century and in France after the revolution.[13] There is no knowledge of any other all-comprehensive and well integrated approach to mental patients previous to that of Chiarugi, so that his work constitutes a definite landmark in the history of psychiatry. It is unfortunate that statistical figures concerning the patients treated at the Hospital Bonifacio are not available and that Chiarugi's work remained interrupted at his death by a lack of a successor. Even more unfortunate is the fact that Chiarugi's name was soon forgotten in the midst of the political turmoil created by the wars of independence in Italy during the past century and that his book, written in a language not known to many, remained virtually inaccessible to many. As shown by the well-documented studies by E. Padovani[14] and G. Mora,[15] Chiarugi's reform was largely overlooked not only in this country, but even in Italy, by psychiatrists as well as by medical historians, up until the beginning of this century. The re-evaluation of Chiarugi's work, antedated by a famous polemic article by C. Livi in

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[12] In the historical introduction to his *Traité médico-philosophique* (1801), Pinel passed a very harsh and unjust judgment on Chiarugi's work. Unfortunately, such a judgment was uncritically repeated by later psychiatrists. Actually, the similarities between the two works of Chiarugi and Pinel are striking, especially in regard to the classification of mental diseases and to the treatment of mental patients.

[13] This consideration could be extended also to this country, where the reform of the treatment of mental patients, as introduced by Benjamin Rush and others at the beginning of the 19th century, coincided with a reform movement of the whole social life of the nation. See: A. Deutsch: The Mentally Ill in America, New York: Doubleday, 1937, especially Chaps. 5 and 6.

[14] E. Padovani, Pinel e il rinnovamento dell'assitenza agli alienati . . . , Giorn, psichiatr. e neuropat., **55**: 69, 1927.

[15] G. Mora, Vincenzo Chiarugi (1759-1820). His contribution to psychiatry. Bull. Isaac Ray Med. Libr., **2**: 50, 1954.

1864,[16] officially began at the beginning of this century with the description of Chiarugi's approach to mental diseases by S. Kornfeld,[17] and was followed by the beautiful essay by A. Vedrani[18] and more recently by the above-mentioned studies by E. Padovani and G. Mora. Beside this, Chiarugi's work has been recently the subject of a number of less important articles or of simple mention by some psychiatrists and medical historians. Today, at two centuries from his birth, Chiarugi's reform should be rightly commemorated as the beginning of a new era in psychiatry and his name should be given a proper place in the history of psychiatry.

[16] C. Livi, Pinel o Chiarugi ? newspaper *La Nazione* (Florence), 1864. This paper was re-published several times during the last century in the Italian literature. An English translation of this paper by J. Workman appeared under the title "Life of Chiarugi," Alienist and Neurologist, 3, 93, 1882.

[17] S. Kornfeld, Geschichte der Psychiatrie, in Th. Puschmann's *Handbuch der Geschichte der Medizin*, Jena, Fischer, 1905, vol. 3, p. 639.

[18] A. Vedrani, Vincenzo Chiarugi, in *Gli scienziati italiani dall'inizio del medio evo ai nostri giorni*, Roma, 923, vol. 1, p. 40-44.

PROCEEDINGS OF THE AMERICAN PSYCHIATRIC ASSOCIATION

THE ONE HUNDRED AND FIFTEENTH ANNUAL MEETING PHILADELPHIA, PENNSYLVANIA, 1959

The 155th Annual Meeting was held in Philadelphia, Pennsylvania, April 27-May 1, 1959, with headquarters at the Bellevue Stratford Hotel and business meetings and scientific sessions at the Trade and Convention Center. The opening meeting was called to order by Dr. Francis J. Gerty, President, at 9:00 a.m., on April 27. The Right Reverend William P. Roberts, D.D., former Bishop of Shanghai, delivered the Invocation; His Honor, Richardson Dilworth, Mayor of Philadelphia, gave a welcoming address to the members, followed by the introduction of Dr. William Malamud, the President-Elect, by Dr. Gerty. Dr. Mathew Ross, Medical Director, was called upon to give his first report to the membership since assuming this position. He spoke on the importance of continuing to improve methods of communication within the Association, on his plans for becoming acquainted with more of the membership, and on activities of the Central Office. Dr. Walter Obenauf, Speaker of the Assembly of District Branches, presented his report noting the enlarging scope and responsibility of the District Branches in the activities of the Association. Dr. Theodore L. Dehne, who served as Co-Chairman with Dr. Lauren Smith for the Arrangements Committee, spoke regarding the work of this Committee in handling preparations for the Annual Meeting. In his report as Chairman of the Program Committee, Dr. John Donnelly announced various aspects of the Program of special interest and stated that 174 scientific papers and 26 Round Tables composed the Program for this meeting. Dr. Lawrence C. Kolb, who had been elected by Council to the position of Secretary Pro Tempore due to the illness of the Secretary, Dr. C. H. Hardin Branch, reported that the official membership count on March 31, 1959 was 10,420. The Treasurer, Dr. Robert H. Felix, then reported on the financial standing of the Association at the end of the fiscal year on March 31, 1959.

The Chairman of the Hofheimer Prize Board, Dr. John Nurnberger, announced that the Association's $1,500 prize was presented this year to Irving L. Janis, Ph.D., for his research work published as "Psychological Stress: Psychoanalytic and Behavioral Studies of Surgical Patients." The 1959 recipient of the Isaac Ray Award was Dr. Maxwell Jones, the well-known British psychiatrist, who will present a series of lectures on psychiatry and the law during the coming academic year at the George Washington University in Washington, D. C. Dr. Ross announced the Nebraska Psychiatric Institute as the winner of the 1958 Mental Hospital Service Achievement Award. Honorable mention was also accorded to the Minnesota Department of Public Welfare, St. Paul, Minn., the New Jersey Neuropsychiatric Institute, Princeton, N. J., and Osawatomie State Hospital, Osawatomie, Kan. Recommendations of the Membership Committee, as approved by Council, on applications for election to membership and for changes in membership status were formally presented to the membership for vote and, on motion duly seconded, were approved as presented.

Dr. Malamud then introduced Dr. Gerty who presented his Presidential Address entitled "The Physician and Psychotherapy" in which he provided a careful analysis of the concept of psychotherapy and its place as a treatment method in medicine, including the role of the psychologist in relation to psychotherapy. Dr. Malamud was respondent. Immediately following this address, the session observed a moment of silence in memory of those members of the Association who had died since the 1958 Annual Meeting. Dr. Kenneth Appel then read a Memorial to the late Past-President

Edward A. Strecker.

The second business session was called to order by Dr. Gerty on Tuesday, April 28, at 2:00 p.m. The first item of business was a report of the results of the election of officers for 1959-60. The successful candidates were announced by Dr. John E. Davis of the Board of Tellers as follows: Dr. Robert H. Felix, president-elect; Dr. S. Spafford Ackerly, vice-president; Dr. Franklin Ebaugh, vice-president; Dr. C. H. Hardin Branch, secretary; Dr. Addison M. Duval, treasurer; incoming Councillors: Dr. Calvin Drayer, Dr. Paul Hoch, and Dr. Aldwyn B. Stokes.

Reports were presented by the Coordinating Committee Chairmen reviewing the activities of their respective groups of committees during the past year and plans for the future. Dr. Frank Curran, Chairman, reported for the Coordinating Committee on Technical Aspects of Psychiatry; Dr. Wilfred Bloomberg reported as Chairman of the Coordinating Committee on Professional Standards; and Dr. Paul Lemkau, as Chairman of the Coordinating Committee on Community Aspects of Psychiatry. Dr. Lawrence C. Kolb, Secretary Pro Tempore, then read a series of proposed amendments to the Constitution and By-Laws regarding membership in District Branches. These amendments will be presented to the membership for final consideration on the next annual ballot.

Following the completion of the business meeting, Dr. Gerty presided over the annual Convocation for newly elected Fellows at 3:00 p.m. with Drs. Lauren H. Smith and Theodore L. Dehne serving as Grand Marshals. Dr. Karl Menninger delivered the Fellowship Lecture (Academic Lecture) on "Hope," a thoughtful and stimulating examination of this powerful tool in the doctor-patient relationship.

The next business session was opened at 9:30 a.m. on Wednesday morning, April 29, by Dr. Gerty. Dr. Kolb presented the report of the Secretary outlining the major actions of the Council since the last Annual Meeting. On motion duly seconded from the floor, these matters were approved by the membership. By separate motions, Atlantic City was approved as the site of the 1960 Annual Meeting and the Santa Clara-Monterey Psychiatry Society was approved as an Affiliate Society of the Association. Dr. Gerty then read the names of Officers, Councillors, and Committee Chairmen retiring from office at this Annual Meeting and announced that each would receive a Certificate in recognition of his service to the Association.

The Annual Dinner was held on Wednesday evening at 7:30 in the Ballroom of the Bellevue Stratford Hotel. Dr. Gerty introduced various APA officials and their wives as well as representatives of other national organizations and foreign guests. The Past-President Badge was presented to Dr. Gerty by Dr. Francis J. Braceland. The dinner was followed by dancing until 1 a.m.

The Adolf Meyer Memorial Lecture, another highlight of the meeting, was presented at 9:30 a.m. on Thursday morning. Dr. Grey Walter, head of the Physiological Department at Burden Neuropsychiatric Institute in England, spoke on "Where Vital Things Happen" with Drs. Lawrence Kubie and Karl Pribram acting as discussants.

The final business session was held on Friday, May 1, at 9:00 a.m. At this time, the actions taken by the Council on April 30 were reported by the Secretary Pro Tempore, Dr. Kolb. These actions included the appointment of Dr. Paul E. Huston to fill the unexpired term on the Council of Dr. Addison M. Duval, the newly elected Treasurer, and the recommendation that the membership approve the Rhode Island District Branch as a District Branch of the APA. Both of these actions were approved, and the whole report was accepted by the membership upon motion from the floor. With the presentation of the gavel, Dr. William Malamud was formally installed as President of the Association for the coming year, and he announced the new Officers for the Assembly of District Branches: Dr. Alfred Auerback, Speaker; Dr. John R. Saunders, Speaker-Elect; and Dr. Lester Shapiro, Recorder. After a few brief remarks by the new President, this final session was adjourned. The 115th Annual Meeting was officially closed at 5:00 p.m. on May 1.

SUMMARY OF MEETINGS OF COUNCIL AND EXECUTIVE COMMITTEE, MAY 1958 TO MAY 1959

This report presents in summary form the principal actions of the Council and the Executive Committee at meetings held throughout the year. Many routine matters, such as referrals to Committees prior to definitive actions, are not included. Copies of the full minutes have been forwarded to the officers of each District Branch and Affiliate Society following the various meetings to keep their members informed of the matters that were considered and the action that resulted.

Executive Committee Meetings, June 28, and September 14, and October 31, 1958. Approved the recommendations of the Committee on National Defense for Standards to be suggested to the Civil Aeronautics Administration (name changed to Federal Aviation Agency) regarding the physical and mental examination of applicants for licensure in civil aviation. Approved a sample certificate to be issued to hospitals inspected and approved by the Central Inspection Board. Approved the selection of the State of Illinois as the situs for the filing of the group insurance plan for APA members. Authorized the appointment of a committee to review the Psychiatric Research Fund and APA relations with it. Approved the continuation of the Smith, Kline and French Fellowship Committee for another 3 years. Approved a resolution presented by the Therapy Committee stating: "Whereas scopolamine, if used indiscriminately, can have deleterious effects, be it resolved that the APA recommends that compounds containing scopolamine be dispensed on medical prescription only." Requested that the President appoint a Commission to study the needs and policies representing the standards of the APA in research and treatment in psychiatry and appropriated $7000 for interim financial arrangements for the Commission pending the November meeting of the Council. Recommended that an honorarium of $250 be awarded annually to the Fellowship Lecturer (Academic Lecturer) beginning in 1959. Approved a plan to hold a meeting of State Mental Health Commissioners at the Mental Hospital Institute at no cost to the APA. Authorized payment of bills incurred by the House Committee for renovation of the Central Office in excess of the original budget appropriation. Authorized the House Committee to proceed with the Dedication Ceremony for the Central Office in accordance with its preliminary plans. Authorized the Executive Assistant to sign grant applications submitted by the APA to the National Institute of Mental Health. Authorized the Committee on Disaster and Civil Defense to participate in a seminar on civil defense and disaster, and to seek funds from the Office of Defense and Civilian Mobilization to develop a training film in adjunct with the manuals published by the Committee. Appointed Dr. George Tarjan to the Council to fill the vacancy occasioned by the election of Dr. C. H. Hardin Branch to the office of Secretary. Reaffirmed its approval in principle of a proposed organization for Mental Hospital Personnel under APA auspices. Approved a letter of agreement with Dr. Daniel Blain covering his work with the Manpower Project. Directed that the management of APA funds be referred to the Medical Director and the Treasurer for study in consultation with the Chairman of the Budget Committee and the Executive Assistant. Approved in principle a booklet on mental health in industry prepared by the Committee on Industrial Psychiatry (subsequently renamed Committee on Occupational Psychiatry). Directed that the Committee on Certification of Mental Hospital Administrators be limited to a maximum of 7 members appointed for a 3-year term so staggered that approximately one-third will retire each year, that there should be no consultants to the Committee, and that the Chairman and Secretary be appointed on the same basis as other Committee members. Approved a schedule of regulations to govern reimbursable staff travel expenses as presented by the Executive Assistant. Directed that the Ethics Committee account should be rebudgeted so that a total of $500 be placed at the immediate disposal of the Committee for

official expenses and authorized the Committee to submit a request for a supplemental appropriation if necessary. Authorized the appointment of 3 members of the Committee on Nomenclature and Statistics for a period of 2 years, following which the Committee will revert to its normal size of 6 members. Authorized the Ad Hoc Committee in Liaison with the Canadian Psychiatric Association to meet during the fall Committee meetings. Approved recommendations of the Ad Hoc Committee on Increasing Responsibilities of the APA governing joint meetings between APA Sections and outside organizations at the APA Annual Meeting. Expressed sincere appreciation to Dr. Hugh T. Carmichael for his statesmanship in negotiating with the Joint Commission on Accreditation of Hospitals and for his service to the cause of the hospitalized mentally ill in dealing with the problem of mental hospital accreditation. Authorized the Executive Assistant to negotiate for new quarters for the New York Office in accordance with his recommendation and to sign a 5-year lease for such space.

Council Meeting, November 21-22, 1958. Approved the minutes for Council meeting of May 10, 11, and 15, 1958, as amended. Ratified the actions of the Executive Committee meetings of June 28, September 14, and October 31, 1958. Directed that the situation regarding the proposed Bond-Strecker-Appel Award should be clarified by the Treasurer writing to the attorney for the donor specifying the conditions under which the funds for this award can be accepted by the APA. Authorized the Medical Director to expend such funds in excess of the original budget allotment as are necessary to operate the Central Office economically during the remainder of the budget year. Accepted the proposed expenditures for salaries, the retirement fund, rent for the New York Office, printing of APA publications, and maintenance of the Central Office as recommended by the Budget Committee. Accepted the request for an additional Editorial Assistant in the Mental Hospital Service. Accepted the request for authorization of increased rent for the New York Office. Approved the recommendation that the Medical Director drop from the payroll temporary employees involved in projects terminating during the current fiscal year. Approved a request for a part-time administrative assistant for the Assembly. Did not approve, for the present time, a proposal to establish an active library at the Central Office. Approved the request for a contingency fund of $20,000 for the President and the Council. Authorized the Budget Committee to resume its previous practice of preparing a final budget at its fall meeting for consideration by the Council in order to avoid a second meeting of the Committee. Accepted in principle the recommendations from the Commission on Long Term Policies concerning an early publication journal. Approved the current studies of the Commission on Long Term Policies and expressed hope that all will be worked out soon and brought before the Council in the near future. Approved the request of the Nominating Committee that a statement be printed in the Journal indicating the factors considered by the Committee in preparing the annual slate of Officers and Councillors. Directed that copies of all Nominating Committee reports be compiled for the information of subsequent Nominating Committees. Authorized members of the Commission on Principles and Position on Current Issues on Psychiatry to appear before Congress giving testimony to the best of their ability and knowledge with the advice of the total Commission and the APA Officers. Expressed complete confidence in the Commission with regard to possible testimony before Congress, and indicated that the use of the original $7000 appropriation would be left to the discretion of the Commission in financing its activities. Requested Dr. George S. Stevenson to determine how other organizations deal with the matter of recognizing outstanding services by their members and asked that he bring a recommendation to the Executive Committee which would permit the Association to accord appropriate recognition to its outstanding members within constitutional limitations. Authorized the Medical Director to explore the possibility of incorporating the cost of psychiatric treatments into the Group Health Insurance plan in New York. Requested

the President to appoint an Ad Hoc Committee to investigate all aspects of insurance for APA members and directed that this Ad Hoc Committee develop a program of action for consideration by the Council. Viewed with sympathy the need for funds by the Central Inspection Board for the reinspection of hospitals but felt that it could not assume this responsibility. Expressed a vote of confidence to the Central Inspection Board, Dr. Gerty, and Dr. Hugh T. Carmichael for the fine work they are doing in relation to the situation regarding the Joint Commission on Accreditation of Hospitals. Approved the proposed amendments to the Constitution regarding membership as suggested by the Assembly: Article III, Section 3, and new Sections 12, 13, 14, and 15 of the Constitution and Article V, new Section 3 of the By-Laws. Approved the proposed amendments in Article V of the By-Laws involving proposed new Sections 1, 2, 4, 5, 6, and 7, as suggested by the Assembly, with an addition to new Section 2 to read, "A District Branch may elect as affiliates, physicians practicing or residing in its geographical area who are not eligible for membership in the Branch. Affiliates are not members and will be ineligible to vote or hold office in the Branch." Approved the recommendation of the Policy Committee that funds be authorized for circulation to the membership via the Mail Pouch of cogent portions of a letter from the American Psychological Association regarding the latter's position on certification for psychologists, together with an appropriate introductory paragraph. Approved the application of the Santa Clara-Monterey Psychiatric Society for Affiliate Society status and directed that it be presented to the membership for final vote. Approved in principle the recommendation of the Policy Committee for publication of proceedings of Divisional Meetings at no expense to the APA, with the APA Publications Department functioning in a manner similar to that now followed with respect to the Research Reports. Approved the recommendations by the Ad Hoc Committee on Education in Public Hospitals in Liaison with the American Psychoanalytic Association that the Central Office keep on file a list of psychoanalysts who are willing to participate in an educational program in state hospitals, that this service be publicized in the Mail Pouch, the Journal, and Mental Hospitals, and that the Central Offiice take charge of carrying out this service. Approved the proposed standards for training in child psychiatry as recommended by the Committee on Child Psychiatry and the Committee on Medical Education. Approved the recommendations of the Committee on History of Psychiatry regarding the development of a library in the Central Office, the assembling of archives, records, transactions, and proceedings of the Association, and requested the Medical Director to seek funds for and initate a research project on the historial development of contemporary American psychiatry. Recommended that the Budget Committee consider appropriating $2500 to $3000 for the purpose of beginning a collection of historical material for the Library in the Central Office. Approved the recommendation of the Committee on Medical Education that the *Descriptive Directory of Psychiatric Training in the United States and Canada*, published in 1955, be revised and reprinted on or about October 1960, and authorized the Central Office to carry out the necessary compilation of data and organization of the Directory with editorial assistance as to format, index, and length of descriptions by the Committee on Medical Education. Approved the unanimous sentiment expressed by the Committee on Medical Education that there is no present indication for action on the proposal for adoption of a uniform date of appointment for psychiatric residents, and that the present operation of methods of appointment permits a flexibility which is useful both to the training centers and to the men applying for training. Approved a statement submitted by the Committee on Medical Education regarding the importance of the Conference of the World Medical Association to be held in Chicago in the summer of 1959. Authorized the Committee on Therapy to collect data regarding the amount and type of psychotherapy being done with chronic schizophrenics including a questionnaire to pro-

vide information as to where such psychotherapy has been done. Approved the preparation of a statement by the Committee on Therapy which would endorse the recent statement by the American Medical Association concerning current problems related to hypnosis. Directed that the Committee on Therapy continue to consider the problem of hypnosis with special reference to those matters of particular interest to psychiatrists. Authorized the Committee of Standards and Policies to seek outside funds for a second Conference on Volunteers, the program to be initiated by the APA and co-sponsored by the American Hospital Association, the National Association for Mental Health, the American Red Cross, and the Veterans Administration. Directed that the Committee on Cooperation with Leisure Time Agencies re-submit its request for a change in name with a number of possible alternative names for consideration by Council. Approved the request of the Committee on National Defense that two additional sentences be included in the recommended Standards for the Civil Aeronautics Administration (Federal Aviation Agency) governing mental and physical examination of applicants for licensure in civil aviation. Approved a plan for publishing the proceedings of the Hawaiian Divisional Meeting as proposed by Dr. Alfred Auerback. Accepted the report of the Ethics Committee with thanks, approved the actions recommended by the Committee, and authorized the Chairman to notify each individual of the decision of the Committee in his particular case. Recorded its extreme pleasure with the manner in which the Dedication of the Association's new headquarters building was carried out on October 31, 1958, stated that the arrangements were altogether appropriate to the historic occasion, and asked the Secretary to communicate these sentiments to the APA House Committee who planned the program, to the Central Office staff who executed it, and to Mrs. Henry Laughlin and her Committee of Volunteers who so generously contributed to the success of the occasion. Did not approve a request for the compilation and maintenance by the Central Office of a listing of summer employment in psychiatry for medical students because staff is not available to undertake such an operation at this time. Approved the recommendations submitted by Dr. Daniel Blain regarding the financial arrangements for the Manpower Project with the stipulation that September 15, 1958 be continued as the beginning date for the preliminary contract. Approved in principle a Psychiatric-Psychological Evaluation Program by the United States Information Agency and referred it to the Committee on National Defense for further study. Approved in principle the proposed plan for Alan Gregg Memorial Consultantships in Psychiatry, which would make it possible to utilize fully the abilities and the experience of aging and aged psychiatrists.

Executive Committee Meetings, January 24, 1958 and March 7, 1959. Directed that the two APA members of the Psychiatric Research Fund Council, Dr. Gerty and Dr. Branch, should meet with this Council and proceed according to their best judgment on the proposed dissolution of the Fund and merger with Research In Schizophrenia Endowment. Approved in principle a plan for a Conference on a Restudy of Present Standards which would make recommendations concerning their future development, elaboration, and application. Directed that, in view of the invitation by Canada to the International Congress of Psychiatry, an invitation not be extended by the U. S. A. and that the APA firmly support the meeting in Canada. Approved the appointment of Dr. Francis Braceland, Dr. Winfred Overholser, and Dr. Lothar Kalinowsky to a committee to work out arrangements between the U. S. A. and Canada for the International Congress. Reiterated with enthusiasm its approval in principle of the proposal for the establishment of Alan Gregg Memorial Consultantships in Psychiatry. Expressed its approval of a certificate to be presented to Dr. Seymour Vestermark on March 7, 1959. Requested the President to appoint a Commission on Awards and Recognitions to present recommendations at the Fall Council meeting on proposals for types of awards, format, method of selection, and continuance of the Commission itself. Ap-

proved a restatement by the Secretary of the policy governing joint meetings between APA Sections and outside organizations at the APA Annual Meeting. Directed that the publication of the proceedings of the APA Teaching Institute at McGill University not be underwritten by operating funds of the APA. Approved the revised budget for 1959-1960 as recommended by the Treasurer with expenditures totalling $716,749 and income estimated as $763,125. Approved a proposed plan for coordinating of Journal and Mail Pouch advertising on a one-year trial basis as presented by Mr. Davies with the understanding that it will produce more income for both the Journal and the Mail Pouch. Stated that the APA is not able to participate in a commercially sponsored conference such as the one held by the National Hearing Aid Industry but indicated that the Conference is free to invite members of the Association to participate as individuals. Requested the Medical Director to prepare a letter commending Mrs. Marion Hildebrand for her volunteer work for the Mental Hospital Service. Expressed gratification that the World Health Organization had designated April 7, 1959 as World Mental Health Day, thus giving international recognition to one of humanity's greatest health challenges and furnishing a fitting prelude to World Mental Health Year in 1960. Also directed that this statement be disseminated to the membership and that the Medical Director relay it to appropriate organizations and leaders. Approved the appointment of Dr. Joel Handler as APA representative to a meeting of the Joint Committee to Study Paramedical Areas in Relation to Medicine, held on April 4-5, 1959. Voted that in view of its minimal participation, the APA withdraw from the Psychiatric Research Fund and not continue in any official capacity, and authorized the President and the Secretary, Board members by virtue of their APA offices, to resign from their positions with the Psychiatric Research Fund. Reiterated its approval for the appointment of a committee to review the financial structure of APA insurance plans, with a $1,000 appropriation for committee expenses. Voted to continue the contract with Dr. Daniel Blain for the Manpower Project until June 5, 1959 with some modifications of the original conditions. Directed that an amount not to exceed $2,000 be made available to the Coordinating Committee on Technical Aspects of Psychiatry during the current budget year to defray obligations already incurred and directed that a careful evaluation be made of inevitable expenses for the coming year. Asked the President to appoint a delegate to the International Congress on Mental Retardation to be held in the summer of 1959. Authorized payment of obligations incurred by the Assembly of District Branches in excess of its budget for the 1958-1959 fiscal year. Extended a vote of commendation to Dr. Mathew Ross for his work in stating principles for planning facilities and services for psychiatric care, authorized him to continue with this project together with the American Hospital Association, and to work towards publication of this set of principles in final form. Directed that the Ad Hoc Committee on Relations with the Canadian Psychiatric be dissolved and empowered the President to work with Dr. Charles Roberts on arrangements for a joint committee between the APA and the Canadian Psychiatric Association. Directed that the Medical Director proceed with a plan for obtaining donations of books for the Central Office library and for psychiatric centers abroad. Authorized APA participation in the 1960 White House Conference on Children and Youth and directed that a delegate be appointed and that $100 be contributed to the Conference from the Council Contingency Budget.

Council Meetings, April 25, 26, and 30, 1959. The Council was informed that Dr. C. H. Hardin Branch would be unable to perform his duties as Secretary for several months because of illness. Acting under its authority as the constitutional governing body of the APA, the Council authorized itself to nominate and elect a Secretary Pro Tempore with all the powers and functions of the Secretary until such time as Dr. Branch is again able to assume the duties as Secretary. Elected Dr. Lawrence C. Kolb as Secretary Pro Tempore. Approved the actions of the Executive Committee since the Council meeting of November 21-22, 1958. Recommended acceptance

by the membership of the list of candidates for election to membership or change in status, as submitted by the Membership Committee. Voted that the APA rejoin the National Health Council and authorized the payment of dues to this organization from the Council Contingency Fund. Requested the President to appoint an Ad Hoc Committee to study the proposed addition to the By-Laws dealing with Chapters in District Branches. Directed that Dr. Howard Potter be asked to explore unofficially with the Philippine Psychiatric Association the question of whether that body might wish to make a direct request to the APA that the Philippines be included in the roster of countries served by the Association. Nominated Dr. Jack Ewalt for a term on the American Board of Psychiatry and Neurology to succeed Dr. David Boyd whose term expires December 1959. Directed that the Commission on Principles and Position on Current Issues in Psychiatry concern itself with problems that are relevant to the American Psychiatric Association as a whole and that local problems should be referred to local and District Branch Societies unless the Commission is requested specifically to assist. Requested that Dr. Francis Braceland, Chairman of the Commission, appear before the Assembly of District Branches to explain the above action. Authorized the appropriation of approximately $12,000 per year to employ a legislative aide to work in conjunction with the Commission on Principles and Position on Current Issues in Psychiatry. Approved the continuation of the Commission for another year and accepted its report. Directed, on recommendation of the House Committee, that no portraits be hung in the Modern Founders' Room in the Central Office at the present time. Approved a plan to hang portraits of the 13 founders in the Century Club Room and directed that such portraits should be from 20-24″ wide and 24-30″ high, rectangular or oval, that the frames should be gilded and not wider than 4″, that the portraits need not be uniform in size, style, or medium, and that original portraits are preferred if such are available. Directed that a portrait of Dr. Benjamin Rush, 36″ high and 30″ wide, should be hung in the main foyer of the Central Office behind the receptionist's desk. Directed that photographs of Past-Presidents of the APA should be solicited from the individual concerned or from his family, that such photographs should be approximately 8 inches wide and 10 inches high, with a dull mat finish. These should be presented unmounted and unframed, and autographed. In case the Past-President is deceased, a facsimile of his signature will be reproduced on the photograph from an available copy. Directed the Secretary to write to all Past-Presidents and instructed the Committee on History of Psychiatry to undertake such research as is necessary to obtain a complete set of photographs. These photographs will be hung in the Presidents' Room and/or at such suitable locations as the House Committee may select. Rescinded the Standards for Electroshock Treatment of May 1953. Approved APA membership in the World Federation for Mental Health and authorized payment of membership dues amounting to $92.80. Received a report from Dr. George S. Stevenson on methods of honoring outstanding work by members of the Association. On suggestion by Dr. Blain, requested the President to appoint an Ad Hoc Committee to oversee the handling of funds remaining in the Manpower Project. Approved the recommendation that the Vice-Presidents of the Association be assigned the duty of speaking before the constituent psychiatric organizations of the APA to interpret the policies and actions of the Association and to report the questions and reactions which they so gather to the Executive Committee. Requested the President to appoint an Ad Hoc Committee to review the matter of expenses and speaking engagements of Vice-Presidents. Upon recommendation of the Ad Hoc Committee appointed to study the matter of District Branch Chapters, approved in principle a plan leading to only one District Branch in each State, Province, or Territory, and stated that if it seems desirable, a Branch could organize within its geographical area one or more sub-sections known as Chapters. Referred this proposal to the Assembly for development and expressed the opinion that, in the meantime, new District Branch-

es should not be organized to cover less than a State, Province, or Territory, and that further fragmentation of present District Branches should be discouraged. Recommended that the Ad Hoc Committee to study this matter be continued as long as necessary and directed that it work in cooperation with the similar committee of the Assembly. Approved the signing of checks and the management of APA financial affairs by Dr. Addison M. Duval, the new Treasurer, effective May 1, 1959. Authorized Mr. Austin Davis, Executive Assistant, to continue to sign checks on all checking accounts of the Association, subject to present voucher controls or by any different system of voucher controls adopted by the Treasurer on recommendation of the Auditor. Authorized Mr. Joseph Turgeon to continue to sign checks on the checking account in the Riggs National Bank in Washington, D. C. Authorized the Medical Director and/or the Committee on Grants and Awards to receive spontaneous funds for establishment of a Seymour D. Vestermark Memorial Lecture on the subject of Psychiatric Education. Designated Dr. George S. Stevenson as APA representative to the Second National Conference on World Health in Washington, D. C. on May 7-9, 1959. Elected Dr. William Malamud as Moderator for the Council and Executive Committee for the coming year. Elected Dr. Francis Gerty and Dr. Jacques Gottlieb to serve on the Executive Committee during the coming year. Elected Dr. Paul Huston to the Council to fill the unexpired term of Dr. Addison M. Duval, the newly elected Treasurer. Approved the appointment of Dr. Arthur Unger and Dr. Lloyd Morrow to the Membership Committee. Regarded favorably the work of the Committee on Relations with Psychology and encouraged it to pursue several solutions which the Committee had suggested to resolve the problems existing in this area. Expressed its realization to colleagues in the Canadian Psychiatric Association of their obligation and prerogatives to make the final decision regarding the date of the International Congress of Psychiatry in Montreal in 1961 but expressed the sincere hope that an amicable arrangement can be reached whereby this meeting date will not conflict with that of the World Federation for Mental Health in Paris in August-September, 1961. Directed that the type "D" student fellowships given by the Smith, Kline and French Foundation Fellowship Committee be called "Vestermark Fellowships" as recommended by that Committee. Directed that it be made a rule of the Executive Committee and the Council, to be reconsidered each year, that the Medical Director be present at all Executive Sessions of either body unless specifically directed otherwise. Recommended approval by the membership of the proposed Rhode Island District Branch. Directed that an explanatory paragraph be prepared by the Committee on Constitution and By-Laws in cooperation with the Speaker of the Assembly to accompany the alternate choices for proposed amendment to Article V, Section 2 of the By-Laws. Requested the President of the Association to send a telegram to the North Dakota State Medical Association stating the APA's position regarding the appointment of a nonmedical superintendent to a mental hospital and advising that, in the best interests in the care and treatment of such patients, including the mentally retarded, an adequately trained psychiatrist should serve as the principal administrator. Authorized the appropriation of $150.00 to the Committee on Aging to conduct a re-survey of psychiatric interest and activity in the problems of the aged, utilizing a random sample of 600 members of the APA, to determine any change in attitude or practice since the first survey carried out three years ago. Expressed appreciation for the fine job done by Dr. Frank Curran in his position as Chairman of the Coordinating Committee on Technical Aspects of Psychiatry. Authorized the appropriation of an additional $1000 to the Coordinating Committee on Technical aspects of Psychiatry for the 1959-1960 budget year. Continued the Ad Hoc Committee on Education in Public Hospitals in Liaison with the American Psychoanalytic Association. Changed the Ad Hoc Committee on Increasing Responsibilities of the APA to a Standing Committee on Internal Activities of the APA, with rotating membership, reporting directly to Council. Continued the Ad Hoc

Committee on an Organization for Mental Hospital Personnel for another year. Authorized a change in name for the Committee on Legal Aspects of Psychiatry to the Committee on Psychiatry and the Law. Authorized a change of name for the Committee on Industrial Psychiatry to the Committee on Occupational Psychiatry. Continued the Ad Hoc Committee on District Branch Committees for another year. Authorized the annual appointment of an official liaison representative to the American Bar Association as recommended by the Committee on Psychiatry and the Law. Approved a recommendation for a change in size of the Committee in Liaison with the American Hospital Association to permit six representatives from each organization on the Committee. Approved the recommendation of the Ad Hoc Committee on an Organization for Mental Hospital Personnel that District Branches be encouraged to hold local Mental Hospital Institutes on a trial basis to see if the relations with non-psychiatric hospital personnel under study by this Committee could be thereby established. Authorized the Committee on National Defense to send a letter to the Federal Aviation Agency reaffirming its previous suggestions regarding mental and physical examinations of prospective civilian pilots. Upon recommendation by the Committee on National Defense, voted to record through the Medical Director its regret and objection concerning the extreme limitation of psychiatric treatment in the Medicare Program. Authorized the Medical Director to assist in the establishment of a proposed organization of non-medical mental hospital business managers. Directed that no member of the Council, nor any candidate for this office, should be scheduled on the Annual Meeting program on Thursday.

LAWRENCE C. KOLB, M.D.,
Secretary Pro Tempore

TREASURER'S REPORT : AMERICAN PSYCHIATRIC ASSOCIATION

At the close of our Fiscal Year, which ended March 31, 1959, we find we have been able to live through our most difficult period, financially, without borrowing any money, with a home which is debt free and with assets totalling over ½ million dollars.

On that date our position was as follows :

Cash on hand (including savings accts.)		$ 53,111.32
Accounts receivable		14,109.15
Marketable securities (book value $88,134.60)		152,600.00
Central office land and building at cost	$275,907.30	
Furniture and equipment (Central Office)	15,229.94	
		291,137.24
Total Assets		$510,957.71

$92,430.30 of these assets have been allocated to special purpose and restricted funds, and are therefore not available for other expenditures leaving a balance of $418,527.41. In addition, there is a total of $47,134.76 in cash and securities in Restricted Funds.

Against these assets are liabilities of one type or another of $85,441.62. Also the assets figure contains a paper profit of $64,465.34 on our securities. This figure, of course, fluctuates depending on the market. Our portfolio is sufficiently diversified, however, that, barring a general downward trend in the market, our investments represent a sizeable profit. Also it will be noted that the home and furnishings are carried in this report at cost. This is an extremely conservative figure.

If, then, we deduct our liabilities from our assets, other than those contained in restricted funds, we still have net assets of $333,085.79. The bulk of this consists of our home and our investments.

It may well be asked why our annual budget is so tight if we have assets of this magnitude. It should be remembered that these assets as listed here consist of debt-free property and securities at market value on March 31, 1959. The securities earned the Association $5,864.79 last year. To liquidate

any portion of them will not only reduce our favorable financial position, but will also reduce the income to the Association. To realize cash on our property would either increase our fixed obligations by the amount of interest charged on the loan or it would permanently reduce our financial base by sale of the property. Therefore eating into these funds should be reserved for dire emergencies or as a part of a general program of liquidation.

On the other hand, it appears as though we must budget increased amounts for our fixed expenses in the future over what we have in the past. Costs continue to rise which means that it will cost us more money to do the same things we are doing now. This applies to salaries, utilities, taxes, travel, printing, postage, rent and other items. Fortunately, due to the dedication and skill of our Executive Assistant, Mr. Austin Davies, we have been able to get by during the past year. I can assure you this has required real financial acrobatics.

The membership may find that for the next few years many projects which are desirable and worthwhile may of necessity be deferred until they can be financed within our annual income.

We have come through our most difficult year although the next two or three will also be strenuous, but we are coming out of the woods and, I confidently feel that our greatest and most productive days are still ahead of us.

R. H. Felix, M.D.,
Treasurer

NEWS AND NOTES

Milwaukee Neuro-Psychiatric Society.—The annual meeting of the Milwaukee Neuro-psychiatric Society was held on Wednesday, May 20, 1959. Officers selected for the year 1959-60 are as follows: president, C. J. Buscaglia, M.D.; vice-president, George J. Martin, M.D.; secretary-treasurer, Henry Veit, M.D.; councillors remaining: Edward Carl Schmidt, M.D., and David Cleveland, M.D.

Association for the Advancement of Psychoanalysis, Inc.—On Wednesday, September 30, 1959, the Association will sponsor its regular meeting at the New York Academy of Medicine at 8:30 p.m. Dr. Harold Kelman will present a paper entitled "Separateness and Togetherness." The discussants will be Drs. Jack L. Rubins and Abe Pinky.

American Academy of Psychotherapists.—The fourth annual conference of the American Academy of Psychotherapists will be held October 17-18, 1959, at the Barbizon Plaza Hotel, N. Y. C. The topic is "Divergencies and Agreements in Methodologies of Psychotherapists." Dr. Robert A. Harper will present the theoreticians' viewpoint concerning the 5 schools of psychotherapy which will include the following: Rudolf Dreikurs, M.D. (Adlerian); Jule Nydes (Freudian); Laura Perls, Ph.D. (Gestalt); Carl Rogers, Ph.D. (Client-Centered); and Carl Whitaker, M.D. (Experiential). The dinner speaker will be Leonard Feldstein, M.D., Ph.D. For further information write to: American Academy of Psychotherapists, 30 Fifth Ave., New York 11, N. Y.

Social Legislation Information Service, Inc.—This nonprofit association established in 1944, supported by contributions and subscriptions, reports impartially on Federal social legislation and the activities of Federal agencies affecting family life, children, and community services in the areas of health, education, welfare, housing, employment and recreation. The Service takes no position for or against the legislation reported.

Subscriptions to the Bulletin may be obtained from Social Legislation Information Service, 1346 Connecticut Ave., N. W. Washington 6, D. C. Price: $18.00 per year; single copies 25c.

Clinical Nursing Officer at Saskatchewan Hospital, Weyburn, Sask.—At the second annual meeting of the Saskatchewan Psychiatric Nurses Association held at Valley Centre, Fort Qu'Appelle, June 2-3, 1959, attention was called to the fact that the Organization of the Nursing Service at the Saskatchewan Hospital, Weyburn, was the only one of its kind on the North American Continent. The difference between this organization and other nursing services is the addition of the "Clinial Nursing Officer" whose responsibility is as an advisor and coordinator between nurse, psychiatrist and other departments. This Officer acts in a position of sapiential authority as opposed to the structural authority common to most hospitals and enables nurses to express their ideas on patient care as well as saving the psychiatrist time.

Dr. Tompkins Heads Religion and Mental Health Group.—Dr. Harvey J. Tompkins, director of psychiatry at St. Vincent's Hospital, N. Y. City, has been elected president of the Academy of Religion and Mental Health, succeeding Dr. Kenneth E. Appel, the first incumbent. The term of office is two years.

Mental Health Problems of Aging and the Aged.—The sixth report of the Expert

Committee on Mental Health titled, "Mental Health Problems of Aging and the Aged" (Technical Report Series No. 171) is currently available from the World Health Organization, Palais Des Nations, Geneva, Switzerland. Price : 60c.

Public Health News (New Jersey Dept. of Health).—The June 1959 issue of this publication is devoted to the psychiatric problems of childhood which are covered by 8 contributions (Drs. Senn, Kanner, Gallacher, Rose, Robinson, Brancale, V. Terrell Davis, and Carl E. Wendel).

This symposium offers a valuable survey of the more common psychiatric problems and developments of childhood and adolescence.

Volunteer Services to Psychiatric Patients.—A report of the Conference on Volunteer Services to Psychiatric Patients held in Chicago, Ill., June 12-17, 1958, is embodied in a 124-page book published by the American Psychiatric Association, entitled *The Volunteer and the Psychiatric Patient.*

The 5 chapters contain a description of the types of volunteer services both in and outside of the hospital and further principles for volunteer programs. There is also a bibliography of the literature on volunteers in psychiatric institutions.

The book may be obtained from The American Psychiatric Association, 1700 18th St., N. W., Washington, D. C.

Dr. Edward E. Mayer.—The death of Dr. Mayer, prominent psychiatrist of Pittsburgh and supervising director of the Allegheny County Behavior Clinic, occurred June 2, 1959. He was 82 years of age.

He was a graduate of the University of Pittsburgh in both arts and medicine and had been associated with city and county mental health agencies for almost 60 years. He was a frequent contributor to medical literature and had edited Oppenheim's *Diseases of the Nervous System.*

Dr. Mayer was active as consultant both in private practice and in criminal cases. A sentence of his is worth quoting and giving serious consideration : "It is wrong to think of antisocial behavior as always due to mental illness, and that all delinquents need psychiatric care."

He had served as Medical Director of Fairview Sanitarium and as Associate professor of Psychiatry, University of Pittsburgh ; also as neurologist and psychiatrist to the Presbyterian Hospital and the Woman's Hospital of Pittsburgh, and as psychiatrist to the juvenile court of Allegheny County.

In Dr. Mayer's death Pittsburgh has lost one of her most distinguished and respected citizens and physicians.

American Psychosomatic Society.—The Society will hold its 17th annual meeting at the Sheraton-Mt. Royal Hotel in Montreal, Canada, on Saturday and Sunday, March 26-27, 1960.

The Program Committee would like to receive titles and abstracts of papers for consideration for the program no later than December 1, 1959. The time allotted for presentation of each paper will be 10 or 20 minutes.

Abstracts, of 2 or 3 pages, in 9 copies, should be submitted to Eric D. Wittkower, M.D., Chairman, Program Committee, 265 Nassau Road, Roosevelt, N. Y.

American Neurological Association.—At the 84th annual meeting of the American Neurological Association held in Atlantic City, N. J., June 15-17, 1959, the following officers were elected for the year 1959-60 :

President : Derek Denny-Brown ; president-elect : Harold G. Wolff ; 1st vice-president : Charles Rupp ; 2nd vice-president : Samuel Brock ; secretary-treasurer : Melvin D. Yahr ; editor of the transactions : Melvin D. Yahr ; assistant secretary : Charles H. Millikan.

Dr. Bernard J. Alpers was elected to the Council for 5 years, Dr. Benjamin Boshes

for 2 years, and Dr. Adolph L. Sahs was appointed as a Representative to the American Board of Psychiatry and Neurology.

The following were elected to Active Membership in The American Neurological Association : David B. Clark ; Robert Fishman ; Eli S. Goldenson ; Howard Krieger ; William M. Landau ; Tiffany Lawyer ; Lewis L. Levy ; Leo Madow ; Kenneth R. Magee ; John S. Meter ; Lewis P. Rowland and H. Edward Yaskin.

Elected to Associate Membership were : William S. Battersby and Irving H. Wagman.

Elected to Corresponding Membership : Abraham Mosovich.

The 85th annual meeting will be held June 13-15, 1960, at the Statler Hotel in Boston, Mass.

THE FOUNDATIONS' FUND FOR RESEARCH IN PSYCHIATRY.—October 15, 1959, is the next deadline for receipt of applications for research fellowships in psychiatry, psychology, sociology, neurophysiology, and other sciences relevant to mental health. The following deadline is January 15, 1960.

Applicants for fellowships should have completed their residency training and preferably have had several additional years experience in research. Interdisciplinary research training is encouraged as is additional training in the applicant's own field.

The Foundations' Fund also makes grants in support of research in mental health. Completed applications for research grants-in-aid should be filed not later than December 10, 1959.

For further information write to Foundations' Fund for Research in Psychiatry, 251 Edwards St., New Haven 11, Conn.

AMERICAN ELECTROENCEPHALOGRAPHIC SOCIETY.—The newly elected officers of the American Electroencephalographic Society, elected at the June 1959 meeting in Atlantic City, are as follows :

President : Dr. Arthur A. Ward, Jr., Seattle 5, Wash. ; president-elect : Dr. Jerome K. Merlis, Baltimore, Md. ; secretary : Dr. George A. Ulett, St. Louis, Mo. ; treasurer : Dr. Isadore S. Zfass, Richmond, Va.

WORLD POPULATION AND POTENTIAL FOOD SUPPLY

From the facts presented, it is obvious that the present accelerated upsurge of population in the world cannot be disregarded without disaster. The trends predicted by Malthus are apparent today. The world population has more than quadrupled since 1650, but the average yield of food crops per unit area of land generally have been increased at a much lower rate . . . Some measure of population control is necessary. Mankind ultimately must live within his resources or suffer the consequences of the controls imposed by nature.

—WARREN H. LEONARD,
Professor of Agronomy,
Colorado State University.

BOOK REVIEWS

The Chemical Concepts of Psychosis. Edited by *Max Rinkel* and *Herman C. B. Denber.* (New York: McDowell, Obolensky, Inc., 1958, pp. 485, $7.50.)

This book contains up to date reviews by 54 leaders in the various aspects of this field, and is, therefore, strongly advised for all individuals seeking an understanding of the present frontiers in research in this rapidly advancing area of experimental psychiatry. It begins with Henry Osmond's historical contribution in which Lewin's book, *Phantastica,* a pioneer in psychopharmacology, is noted. Among the path-finding work he considers that of Macht, who was the first to report the possibility of a substance in the serum of schizophrenics different from any found in nonschizophrenic normal individuals. He also quotes the investigations of Hoffer, Baruk, Buscaino, Hofmann, Heath, Hoch, Woolley, Rinkel and Mayer-Gross, and it is significant that each of these leaders reviews his own contributions in the same volume. Winter and Flataker, Streifler and Kornblueth follow the lead originally suggested by Macht and find evidence for chemical differences between the sera of normal controls and schizophrenic patients. The list of papers includes Denber's report concerned chiefly with mescaline-induced changes in human subjects, and Evarts' electro-physiologic and behavioral studies of psychotomimetic drugs. Cerletti emphasizes the very small fraction of LSD that enters the brain and Brodie evaluates the role of serotonin as a chemical transmitter. Other experimental work was done on humans by Sherwood, on animals by Feldberg and Marrazzi, and on brain tissue by Bogoch. In all these instances suggestive conclusions are drawn on possible chemical deviations in schizophrenia. The Austrian psychiatrists, Hoff and Arnold, present an amazing analysis of the unsettled problem of schizophrenia and the thoughts of Brill, the Sacklers, Kline, Reiss and Letemendia are all of value to anyone concerned with progress in the organic approach to psychiatry. Block presents a striking suggestion that schizophrenics are victims of chronic poisoning. In contrast to normal individuals in whom the incorporation of amines into proteins is prevented, such an incorporation takes place in schizophrenic patients who are, therefore, subjected to the toxic effects of amino proteins.

The last article is that of Gilbert Cant, who presents a nontechnical review of the volume's contents and explains to the reader not versed in biochemistry the meaning of the new results. It is hoped that enough has been said in this brief review to convince the potential reader that he can acquire a more than passing facility with this many-faceted biochemical attack in psychiatry by perusing these important papers and reviews in this carefully edited volume prepared in an attractive and readable format.

Harold E. Himwich, M.D.,
Galesburg State Research Hospital,
Galesburg, Ill.

Communication, Organization, and Science. By *Jerome Rothstein.* (Indian Hills, Col.: Falcon's Wing Press, 1958. pp. 110. $3.50.)

The steadily increasing implications of information theory for the biological sciences (as evidenced in the fields of genetics, immunochemistry, and neurophysiology), make the appearance of a book such as this a timely event. Although written by a physicist (and carrying a long and scholarly foreword by a fellow physicist) the range of this book is of the widest. It starts with a consideration of the relation of the process of information to entropy, and goes on, by way of chapters on Measurement and Communication and their relation to Thermodynamics, to a discussion of the essential elements of language, and the processes partaking in the construction of scientific theory. The last chapters are devoted to an application of the "Organization Concept," as developed by the author, to the Theory of Games, and the behavior of organized mechanisms in random game situations. It ends with a tantalizingly brief statement of minimal desiderata needed for the construction of the universal medium of communication (*i.e.* a universal scientific language), and with a forceful Credo looking towards a "Unified World Outlook."

In the welter of ideas propounded by the author with clarity and elegance, the nonmathematical psychiatric reader can but select a few items which point to his own subject. One is the argument, advanced in the foreword by Dr. Muses, and extended subsequently by the author, for a need for the conceptualization of the topology, *i.e.* struc-

ture, of Time. This intra- and inter-connectivity of time points and time intervals Dr. Muses names 'Chronotopology.' "The appreciation of time intervals are merely the measure of time ; they are no more time than rulers are what they measure. Of the nature and structure of time itself investigators have all but been silent." One would fully endorse this view, and note the strange way in which this, as yet undeveloped, area provides a meeting ground between the physicist and the sensory physiologist. For both are becoming increasingly cognizant of the way in which a structuring of events in time (in terms of probability) defines these very events, and makes possible their manipulation. In neurophysiology, as in physics, the time dimension is replacing the older dimension of space, an evolution not unlike that undergone by physics towards the turn of the present century.

The ideas proposed by Dr. Rothstein lead on naturally from the ideas outlined in the foreword. Starting with Boltzmann's discovery of the statistical explanation for thermodynamical entropy, he examines entropy as a measure of information by the selection of a message. "Selection of a subensemble from a given ensemble generates an amount of information equal to the difference of the entropies of the two ensembles." This "Set" and "Subset" view he applies successively to the concepts inherent in logic, and the evolution and structure of language as a means of obtaining, and communicating, meaning. The argument is fluid and alive, and ultimately leads to a discussion of organization of data by machine, including the "Well Informed Heat Engines" developed in living matter at macromolecular level. Pervading the argument is the concept of the isomorphs ; the best information-machine we are making, and are likely to make, is built on specifications not unlike the strange molecular machines which make up the very stuff of life.

Whether the coding and memory machines which Dr. Rothstein envisages for the future will indeed expand or contract our lives or the lives of our successors, the message of this essay is clear and relevant. The mathematical and engineering techniques hitherto only inadequately applied to biology may hold profound implications for neurophysiology, psychology and psychiatry. Their core is the structuring and relatedness of events to time, and the provision of adequate techniques for their apprehension and their analysis. Whether we like it or not, the tide of a major scientific evolution is flowing through the Behavioral Sciences ; Dr. Rothstein does them a service by charting their currents in his clear and incisive way.

ADDISON M. DUVAL, M.D.,
Saint Elizabeths Hospital,
Washington, D. C.

LA SCHIZOPHRENIE. By *Guy Delpierre.* (Geneva : Chas. Fomara, 1957, pp. 109.)

This small monograph consisting of 7 chapters is from the International Institute of Psychology and Psychotherapy. Several definitions of the term "schizophrenia" are given including those of Bleuler, Deny, Levy-Valensi, Kretschmer and Claude, the psychogenic and neurogenic factors of etiology are emphasized and the symptoms are enumerated and classified.

In the chapter on dissociation the author points out the differences between this reversible phenomenon and "dementia" and describes the "vital difficulties" the patient has with eternal reality, with the body image (the "mirror sign" is given a special consideration), and with the affective, intellectual and interpersonal components of dissociation.

Three of the Kraepelinian types of clinical constellations are presented, namely, hebephrenic, catatonic and paranoid with their differentiating characteristics. A chapter on the development of the disorder is given with the differential diagnosis from known brain diseases and psychoneuroses and one on pathological anatomy with the comments limited to the histopathology and disturbed neurophysiology of the brain structures.

The 9 pages devoted to therapy considers very briefly the methods of Federn, Fromm-Reichmann, Melanie Klein, Rosen and Sechehaye.

Since there is no author's preface or foreword, the reasons for writing are not quite clear ; however as a condensed text it may be useful to teachers of psychiatry who wish to make a brief review of the phenomenologic aspects in preparing class material. The bibliography (45 items) refers very largely to French sources, but a considerable number of other authorities are quoted without references.

NOLAN D. C. LEWIS, M.D.,
Princeton, N. J.

IN MEMORIAM

KONSTANTIN MIHAILOVICH BYKOV

My first memory of Bykov is that of meeting him in Pavlov's laboratory in the Institute of Experimental Medicine, Petrograd, 1922, and my last when I bade him goodbye as he was leaving the United States in June 1958. After Pavlov, he has done perhaps more to advance the experimental science of the conditional reflex than has any other of Pavlov's pupils. His death in May 1959 in his early 70's removes the best known of the pupils of Pavlov.

Like Lomonosov and many other Russian scientists, Bykov was of humble origin, and like Pavlov he was educated for the priesthood. After studying medicine, he worked with two distinguished Russian physiologists, Pavlov and Ukttomsky, the neurophysiologist. Most of his life was devoted to a steady and unremitting expansion of the investigation of the conditional reflex concepts, by thorough, well designed, and laborious experimentation on the interrelation of the viscera and their adaptation to the external and the internal environment through the mechanism of the conditional reflexes. This work was summarized in *The Cerebral Cortex and the Internal Organs* (New York, 1957, tr. by Gantt). For several decades he worked tenaciously and patiently as a pioneer and almost alone in this field, assisted and encouraged by his wife. However with the gradual increase of funds accorded scientists by the Soviet government, he expanded his physiological department at the Academy of Sciences, Leningrad, which with its branch at the subsidiary genetic laboratory in Koltushi, became the second largest research institute in the Soviet Union, having on its staff a total of 700, 200 of whom were scientists. He studied practically all the important viscera in connection with their acquisition of conditional reflexes and their inter-relations, viz. the interoceptive conditional reflexes.

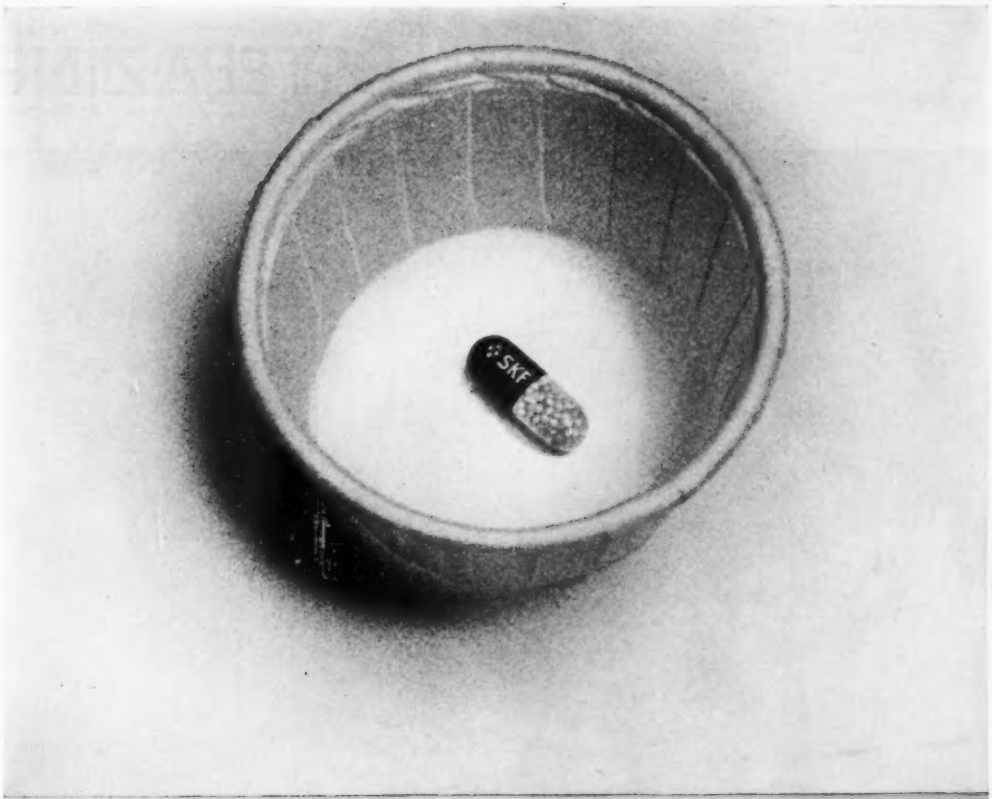
Bykov became the spokesman for Pavlovian physiology after Pavlov's death. This was done through a firm belief in the soundness of the teaching of his master.

Although he stood at the pinnacle of his profession in Russia, he was never extravagant in his own claims, and accorded the most credit for his concepts to Pavlov. He was not a member of the Communist Party and to the best of my knowledge he kept his science free from subservience to politics. Outspoken in his criticism and opinion, he was nevertheless conservative.

A year before his death, he visited the U. S. A. for the first time, at the invitation of the American Psychiatric Association and of the International Gastroenterological Society, speaking before these bodies in San Francisco and in Washington, lecturing en route to the students of Dr. Magoun, in Los Angeles, at Little Rock and at the Johns Hopkins University.

Bykov's sojourn of 5 weeks in the U. S. A. had the double effect of changing his point of view about our country and our opinion of the Russian scientists. He said that when he came here, owing to the articles of Ehrenburg, he expected to be stoned, and that he was amazed to find conditions so different from what he had imagined. His simplicity, humor and genuine courtesy spread an aura of charm everywhere he went. He was described as an "honest and upright gentleman, distinguished and dignified looking, and in his behavior he was the antithesis of what we have been led to expect from Soviet Russia" (John E. Peters). The American Psychiatric Association honored him by proposing him as an honorary member, the first from the USSR. His wife was killed in an automobile accident two years ago. He is survived by a devoted daughter, Tamara, a musician in the Leningrad Theater. His friendly and sparkling humor shining through a dignified mask impressed all those who met him here, and converted even the most obdurate to feel the force of the potential friendship of the scientists of his country and ours.

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Rudy, L.H.; Rinaldi, F.; Costa, E.; Himwich, H.E.; Tuteur, W., and Glotzer, J.: Trifluoperazine in the Treatment of Psychotic Patients, Am. J. Psychiat. *115*:364 (Oct.) 1958.

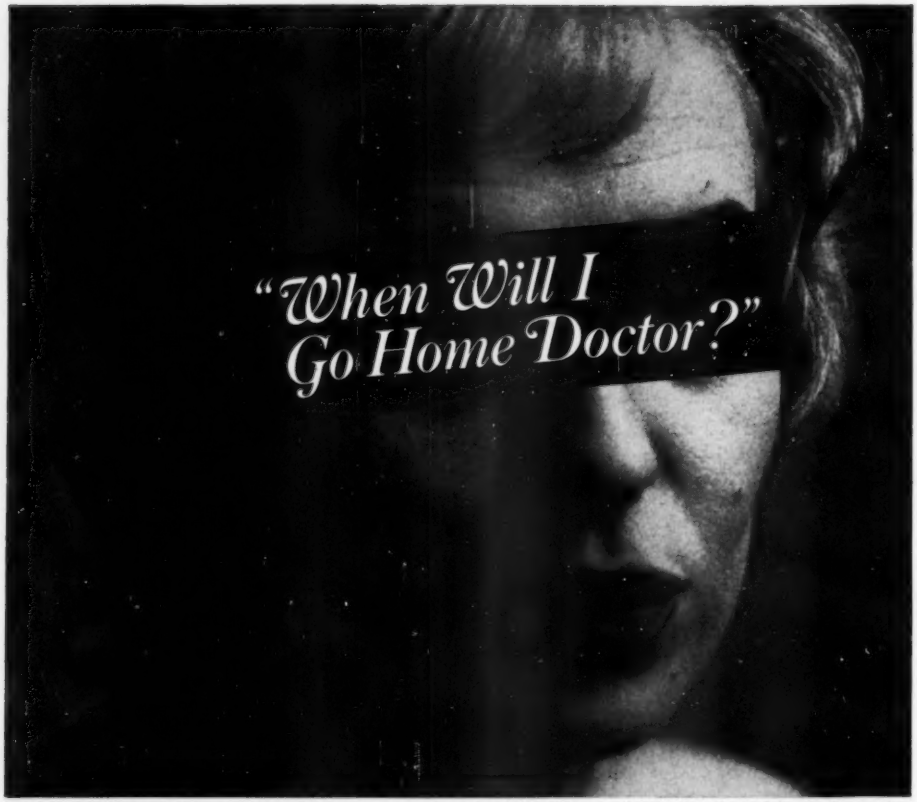
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Madgwick, J.R.A.; McNeill, D.L.M.; Driver, M., and Preston, G.C.: 'Stelazine' (Trifluoperazine), A Preliminary Report on a Clinical Trial, J. Ment. Sc. *104*:1195 (Dec.) 1958.

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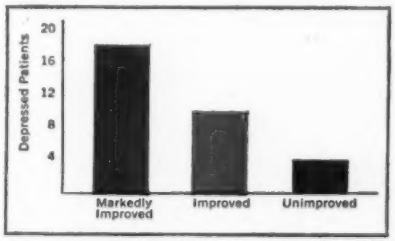
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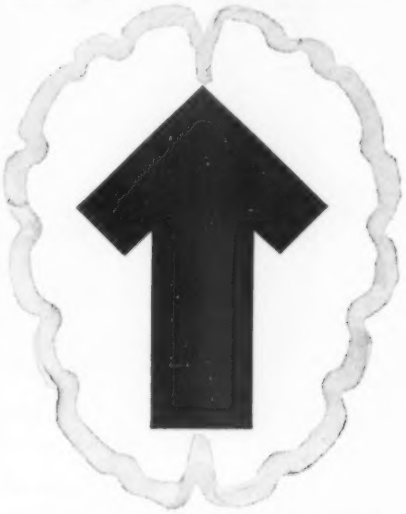
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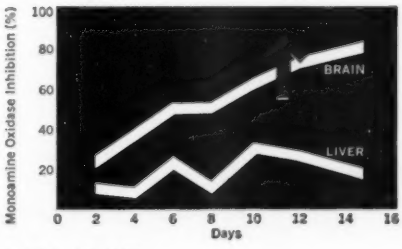
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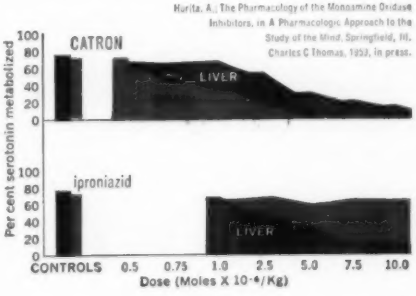
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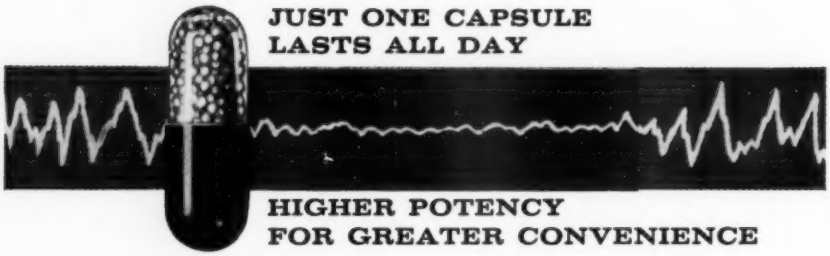
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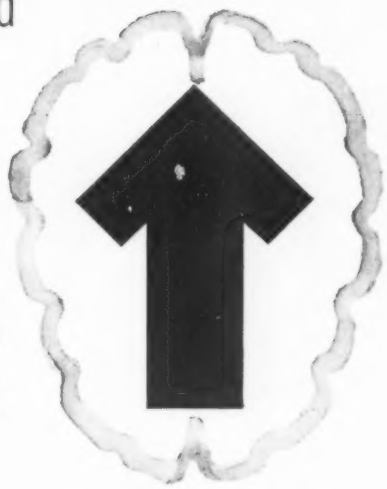
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TYPE OF PATIENTS	Depressed, chronic psychotic patients, mostly schizophrenic (hospitalized)	26 psychotic depressions, manic-depressive and involutional; 9 neurotic depressions (private practice).	36 involutional depressions, av. age 77 (custodial patients in nursing home); 16 reactive depressions, av. age 65 (private practice).
DOSAGE	1-4 tabs. q.i.d. (av. 2 tabs. q.i.d.)	1-3 tabs. q.i.d.	1-2 tabs. t.i.d. or q.i.d.
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RESULTS	Substantial improvement in 41%; some improvement in an additional 39%.[1]	Complete or social recovery in 57%.[3]	Good results in 78% of involutional depressions and in 69% of reactive depressions.[2]

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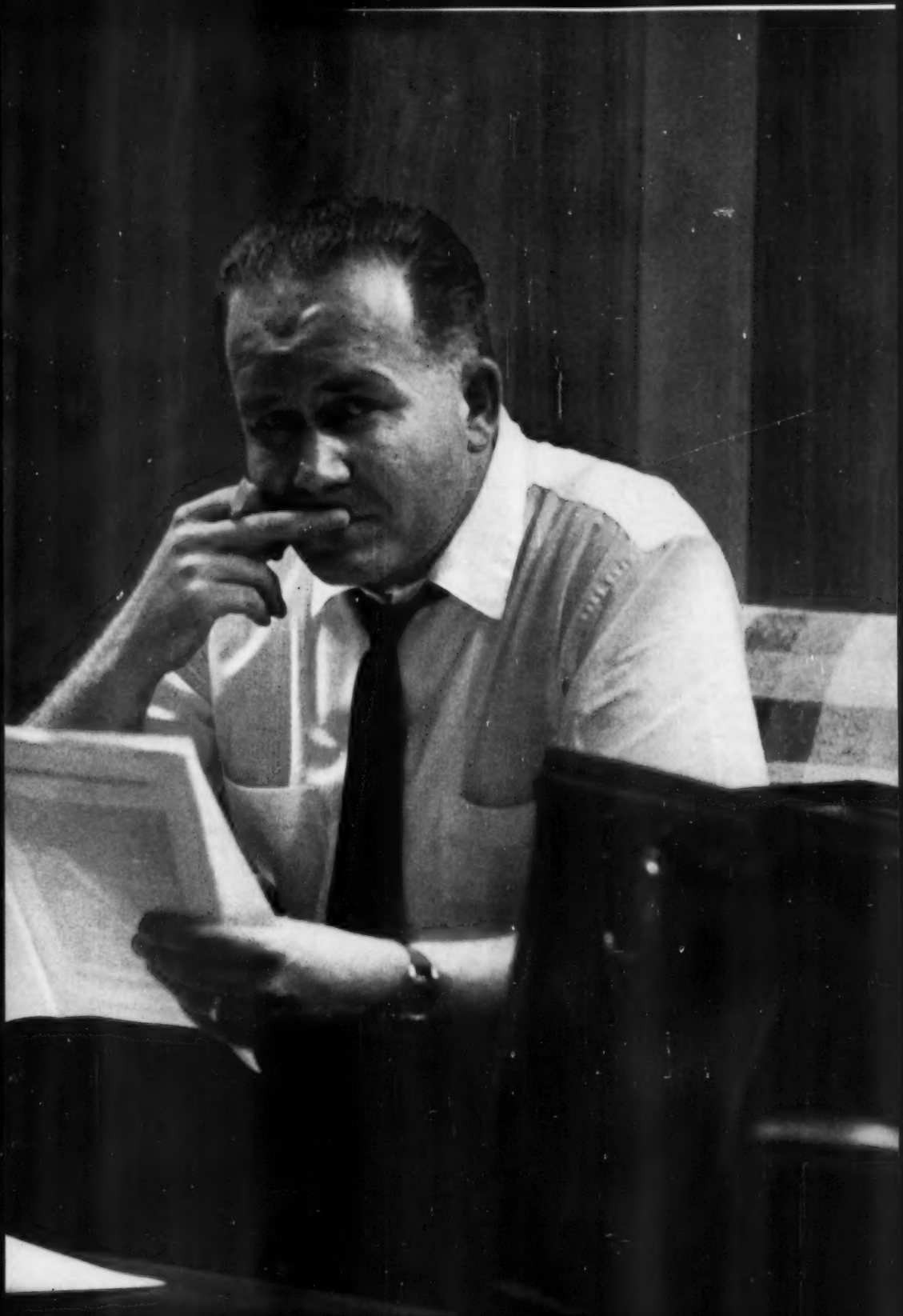
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The clinical record of Marplan—Marplan has been under intensive clinical investigation for more than a year. A broad clinical research program continues to define the full range of Marplan's therapeutic applicability. However, already almost 300 research clinicians have evaluated Marplan in over 3500 cases.[1-8] Of this group, more than 2751 were patients with psychiatric and emotional disorders associated with depression. In the 2449 fully evaluated cases, the greater majority (66.2%) showed significant improvement. "Depression of mood and somatic preoccupation were less pronounced, concentration improved, irritability lessened and the patients appeared to be more relaxed."[2] Marplan was evaluated clinically for more than one year. In some patients, the beneficial effects appeared within several days; in most, within one to three weeks. In a few cases, response was not observed until after three to four weeks of therapy. An example of an unusal result in a chronic psychiatric patient is the following case history from the Danvers State Hospital, Hathorne, Massachusetts[3]:

40-year-old male schizophrenic. *First hospitalized 19 years ago. Continuously hospitalized for the last 10 years. ECT and various phenothiazines proved ineffective. Patient's condition varied between catatonic posturing and actual stupor, and between extreme block and complete mutism. He had no apparent affect. On treatment with Marplan (40 mg/day), he became cheerful, talkative, no longer a feeding problem. Now works in one of the hospital's departments and has ground privileges. Mental content and sensorium disclose no psychotic manifestations at present.*

Incidence of side reactions—In one of the largest bodies of clinical material for this new class of drugs, Marplan shows one of the lowest recorded incidences of side effects. Particular attention was focused on attempts to define as precisely as possible amine oxidase inhibitor side effects on a wide range of organs, including liver and bone marrow. Extensive clinical studies have revealed no jaundice or liver damage attributable to Marplan. Nevertheless, since Marplan is an amine oxidase inhibitor, the same precautions should be observed with Marplan therapy as with other amine oxidase inhibitors.

Marplan, an analog of Marsilid (iproniazid), is a potent new amine oxidase regulator. Already evaluated in over 3500 patients, Marplan has demonstrated marked beneficial effects in the treatment of moderate to deep depressions. Evidence to date indicates that Marplan may also be therapeutically valuable in a number of important acute and chronic medical conditions. Chemically, Marplan is 1-benzyl-2-(5-methyl-3-isoxazolylcarbonyl) hydrazine.

Dosage: As with other potent drugs, for maximum therapeutic effect, the dosage of Marplan must be adjusted for the individual patient. Since Marplan has a cumulative effect, dosage should usually be reduced to maintenance levels as soon as clinical improvement is observed. Many patients may respond to Marplan within a week or less. On the other hand, since Marplan acts indirectly (by affecting enzyme metabolism), a beneficial effect may not be seen in some patients for as long as three to four weeks.

Dosage Schedule: (1) Starting dose is usually 30 mg daily, given in single or divided doses. The patient should be observed carefully and individual dosage adjustment made according to response. Many patients will respond quickly to the initial dose of 30 mg daily. Since daily doses larger than 30 mg may cause an increase in side effects, it is not recommended that higher dosages be employed routinely. (2) Maintenance therapy should be instituted when a therapeutic response has been established, by reducing Marplan to 10 or 20 mg daily (or less). In some patients, beneficial effects may not be observed for three to four weeks.

The same dosage range is also indicated in depression associated with such chronic disorders as rheumatoid arthritis and also for the clinical indication of severe to intractable angina pectoris.

Caution: All patients treated with hydrazine derivatives should be kept under close medical supervision. The patient should be observed for signs of orthostatic hypotension, complaints of dizziness and vertigo, constipation, overactivity, jitteriness, insomnia, peripheral edema, weakness, fatigue, dryness of the mouth, blurred vision and skin rashes. While there is no definite knowledge of a hazard with Marplan, use of this class of agent should be discontinued at the first sign of jaundice or impaired liver function. Periodic liver function tests are advised during hydrazine therapy. These drugs are contraindicated in patients with a history of previous liver disease or impaired liver function. In patients with impaired kidney function, Marplan should be used cautiously to prevent drug accumulation and should not be used in epileptic patients. Patients receiving a hydrazine in conjunction with drugs such as alcohol, barbiturates, meperidine, cocaine, procaine, and phenylephrine should be more closely supervised.

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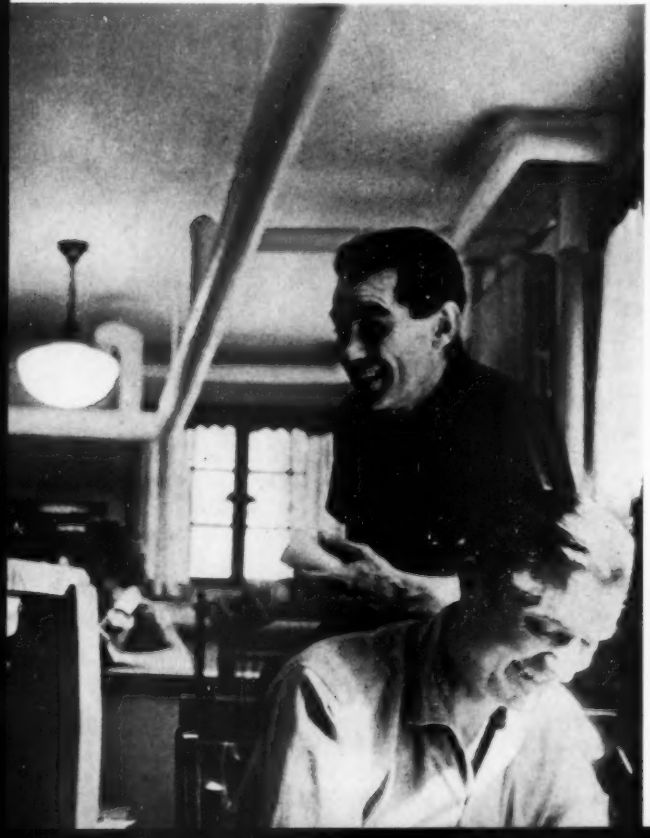






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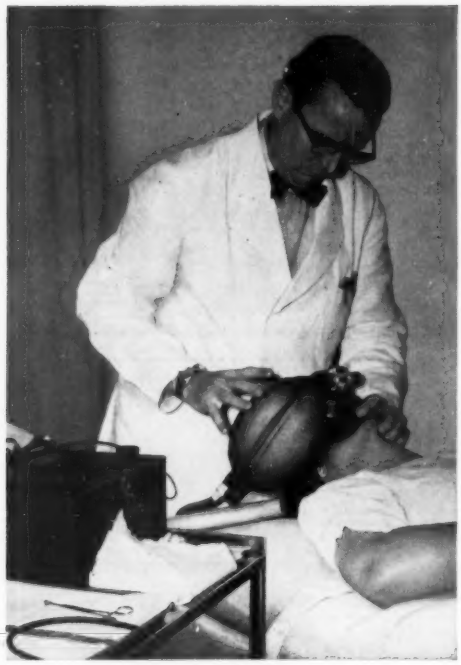
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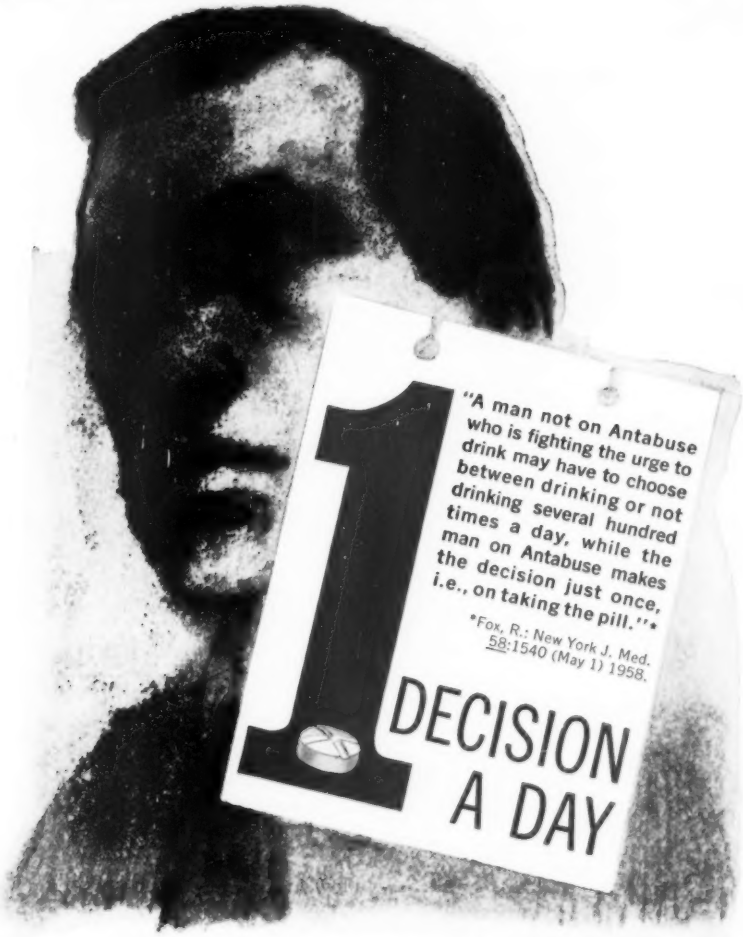
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